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THE BASAL METABOLISM OF PREMATURITY

II. RELATION OF BASAL METABOLISM TO CALORIC INTAKE AND WEIGHT CURVE *

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MARGARET E. MORIARTY AND ALICE J. DALRYMPLE

BOSTON

Scattered through the literature of basal metabolism there are isolated reports of the metabolism findings of premature infants, but up to date no series of cases has been studied consistently showing the characteristics of this type of infant.

We are presenting in this communication the basal metabolism of seven of the twenty-two premature infants studied by us during the past year and a half, in its relation to the caloric intake and the weight curves. A search of the literature gives much data in regard to the caloric intake and requirements of premature infants but in no instance have the caloric intake and the basal metabolism been recorded for the same infant.

The source of the material used was the Boston Lying-In Hospital and the Children's Department of the Massachusetts General Hospital. The subjects were all examined physically, were all organically sound, but had the characteristic appearance of premature infants, and, so far as we were able to determine, were prematurely born from one to two months.

These premature infants had high pulse rates, unstable temperatures, and were at first too weak to nurse the breast. They were consequently either fed by a Breck feeder or by tube. Breast milk was given whenever possible, but, as the supply was not unlimited, it was often necessary to supplement dilute cow's milk formulas.

They were kept in a warm premature room in which the temperature ranged between 72 and 80 F. (from 24 to 26 C.), and cared for with the usual precautions, taken with premature infants.

The blood Wassermann done on the placental blood of the mothers was, in all instances, negative.

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* Received for publication, May 30, 1922.

* From the Children's Medical Department, Massachusetts General Hospital.

These seven babies left the hospital in good condition, and some of them are still under observation.

The technic of the metabolism measurements made in this investigation was that previously described by Benedict and Talbot,[1] with some modifications. These modifications were due, primarily, to the fact that it was necessary to have a higher temperature in the respiratory chamber than was usual with older infants. Furthermore, the small size of the infants studied necessitated the measuring of smaller amounts of carbon dioxid and oxygen than were measured in larger infants. Great experimental care was taken to minimize the errors which might arise under these circumstances.

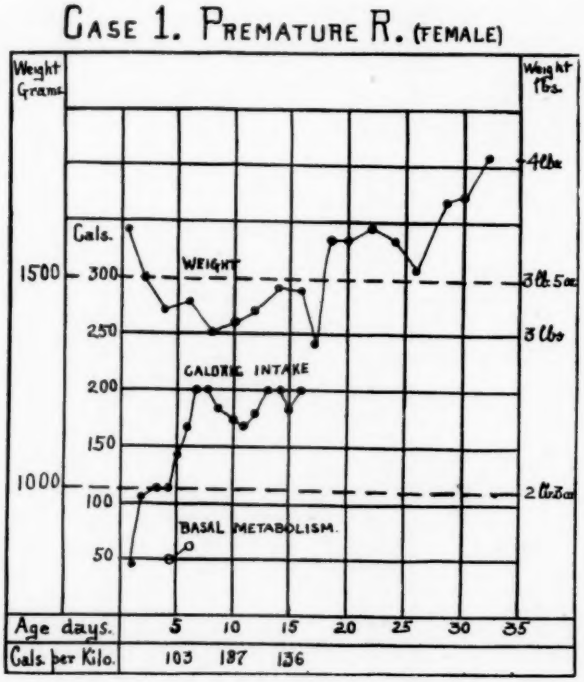

Chart 1.—Case 1. Premature R (female).

The results showed surprising conformity and we feel certain that there were no more variations in the metabolism findings than had been previously obtained in the studies of the new-born infants.[2] All possible factors were controlled, and the periods of observation were made as long as was consistent with the well being of the infant.

Charts 1 to 5, showing our findings in these subjects, were all treated in the same manner; the upper curve representing graphically

1. Benedict and Talbot: Carnegie Institution of Washington, D. C., Pub. No. 201.

2. Benedict and Talbot: Carnegie Institution of Washington, D. C., Pub. No. 233.

the gain in weight, and the middle curve the total twenty-four hour estimated caloric food intake. This latter curve represents the food intake with as much accuracy as could be expected under the circumstances, when the food was not analyzed chemically. The lower line shows the total basal metabolism for 24 hours as measured in a respiratory chamber.

REPORT OF CASES

CASE 1 (R).—Metabolism was done on the fourth and sixth day of life and showed surprisingly low basal figures, that is, from 46 to 56 calories in

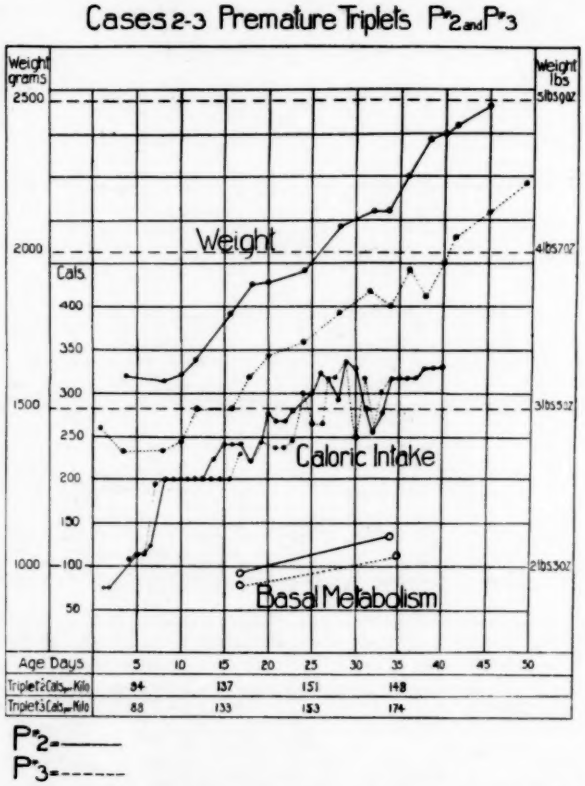

Chart 2.—Cases 2-3. Premature Tripets, P No. 2 and P No. 3

twenty-four hours. The caloric intake at that time was 120 calories, or about double the basal, and, as shown by the chart, the infant continued to lose weight until the eighth day at which time he received 200 calories in the day, or more than three times the basal requirements. This figures approximately 130 calories per kilogram of body weight.

It is an open question whether the initial loss of weight would have occurred in this infant had he been able at first to digest the 200 calories he later gained on.

CASES 2 AND 3 (P 2 and P 3).—These infants were two of triplets. They showed a corresponding similarity between their body weight and basal

metabolism; the larger infant having a higher basal metabolism than the smaller infant. Both started to gain when their caloric intake reached a total of 200 calories a day; P 2 gaining on 122 calories per kilo, and P 3 on 149 calories per kilo.

These two cases serve as an excellent example of the fallacy of estimating the caloric requirements of infants per unit of body weight. A discussion of this problem will form part of a later communication. The total caloric intake of these two infants was close to two and

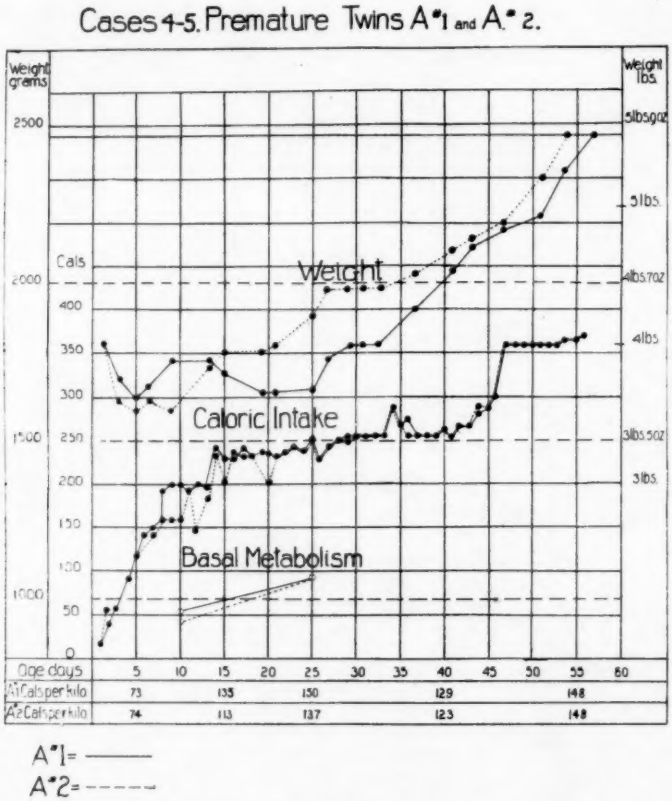

Chart 3.—Cases 4-5. Premature Twins, A No. 1 and A No. 2

one-half times their basal requirements on the seventeenth and thirty-fifth days of life; the calories per kilo rising very rapidly to more than 125, and, toward the end of the observed period were between 120 and 150.

CASES 4 AND 5 (A 1 and A 2; twins).—These infants also had a low total basal metabolism which increased rapidly as they grew older. A 1 did not maintain a consistent gain in weight until after the twenty-fifth day of life when he was receiving a total of 250 calories or 155 calories per kilo. A 2 commenced to gain on the ninth day on a total of 200 calories, 155 calories per kilo, or about two and one-half times the basal metabolism.

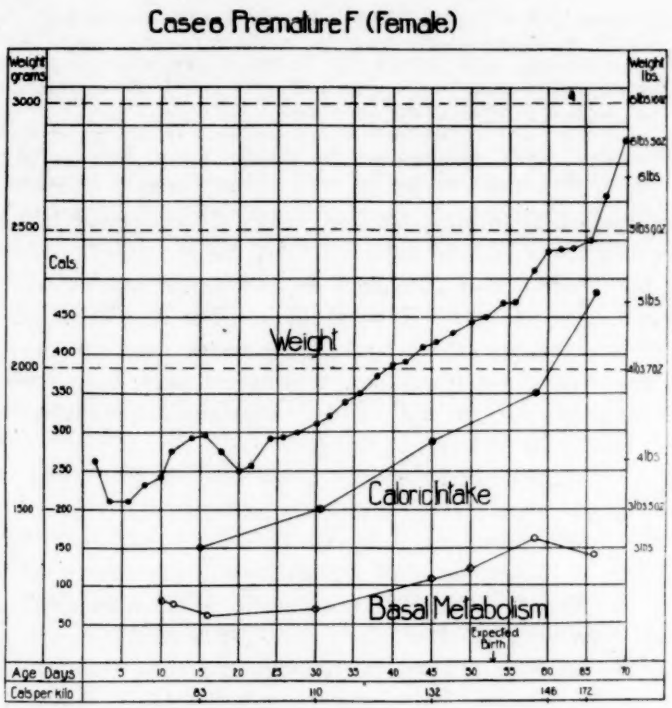

Chart 4.—Case 6. Premature F (female).

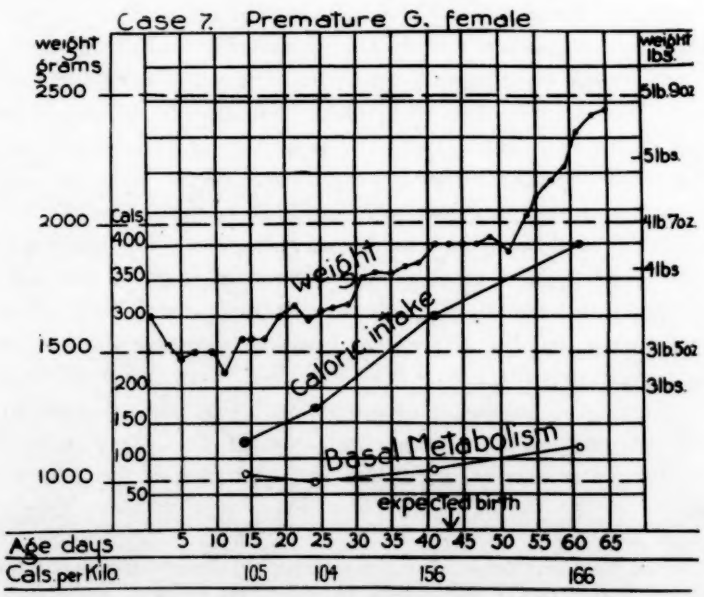

Chart 5.—Case 7. Premature G (female).

CASES 6 AND 7 (F and G).—These babies were studied over a much longer period of time and confirm the findings in the preceding cases. In Case 6 there was an increase of 71 per cent. in the basal metabolism and an increase of 230 per cent. in the caloric intake, with a resulting increase in weight of 58 per cent. over a period of fifty-one days.

In Case 7 there was an increase of 110 per cent. in the basal metabolism and an increase of 190 per cent. in the caloric intake, with an increase of 41 per cent. in the weight during the seventy days under observation.

It is interesting to note that the greater the difference between the basal requirements and the caloric intake, the greater the weekly gain in weight. There is also a tendency for the caloric intake to reach close to two and one-half times the basal findings before a satisfactory gain in weight is obtained. The record of the caloric intake in Cases 6 and 7 was recorded only a few times, at different ages, but shows that a continuous gain in weight did not result until the babies received a total of from 150 to 200 calories in the food.

Satisfactory gains in weight were not made in this series of cases until the babies were able to digest approximately 200 calories in the day. The caloric intake per kilogram of body weight was high in all cases. This is in keeping with the findings of previous investigators: Czerney and Keller, from 110 to 120 calories; Oppenheimer, Langstein and Meyer, from 120 to 130 calories; Salge, from 130 to 150 calories, and Samelson, from 115 to 150 calories.[3] J. H. Hess[4] found that infants weighing from 1,000 to 1,500 gm. had a caloric intake of from 115 to 170 calories per kilo, and infants weighing from 1,500 to 2,000 gm. had a caloric intake of from 102 to 132 calories per kilo.

The basal metabolism determinations in our series of cases was strikingly low no matter how they were charted.[5] This low metabolism seems to be dependent upon the fact that there is a very small amount of active heat forming tissues in these incompletely developed infants.

This evidence is contrary to the generally accepted belief that the heat value of the metabolism is proportional to the body surface area. Premature infants apparently only produce as much heat as is necessary for their well being in the most advantageous surroundings.

It is a well known fact that deprivation of external warmth from premature infants results in a subnormal temperature. We believe that this is evidence that the active heat forming "protoplasmic" tissues are unable to respond to the excessive heat loss from the body, and, as a result, there is a subnormal temperature; that the amount of heat formed depends on the amount and tone of the active protoplasmic tissues and not primarily on the size of the surface of the body of these infants.

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3. Quoted from von Reuss: Die Krankheiten des Neugeborenen, Berlin, 1914.
4. Hess, J. H.: Am. J. Dis. Child. **11**:302 (April) 1911.
5. Talbot and Sisson: Proc. Soc. Exper. Biol. & M., April, 1922.

Close observation of premature infants shows very little muscular activity, and we have been unable to obtain any data which would lead us to suppose that the heat used up in muscular exercise in premature infants during the day was more than 10 per cent. over the basal metabolism. The loss of calories in the excreta of infants is usually less than 10 per cent. of the food intake, unless there are from four to five large curdy stools a day in which case the loss may be as high as 20 per cent. There is left, therefore, a proportionately large number of calories for growth. This is shown very well in the two cases followed over the longest period of time, that is Cases 6 and 7.

CONCLUSIONS

1. The basal metabolism in this series of premature infants was strikingly low.

2. They did not gain in weight until they were able to digest approximately 200 calories in the day.

3. The only food completely assimilated to accomplish this was human milk.

4. A relatively large proportion of the food intake goes to form new body tissue. The large excess of the caloric intake over the basal metabolism was necessary because of the relatively greater amount of growth essential for the normal development of these babies.

INFLUENZAL MENINGITIS *

T. M. RIVERS, M.D.
BALTIMORE

Meningitis produced by *B. influenzae*, although not extremely common, occurs frequently enough to be of considerable interest. According to Dunn [1] and Neal [2] it ranks fourth in order among the types of purulent meningitis, as shown in Table 1.

TABLE 1.—INCIDENCE OF INFLUENZAL MENINGITIS

Type of Meningitis	Dunn's Figures	Neal's Figures
Meningococcic	60	541
Pneumococcic	12	61
Streptococcic	6	49
Influenzal	4	32

In Baltimore, since 1913, at least twenty-three patients with influenzal meningitis have been seen, twenty of whom were on Dr. Howland's service in the Harriet Lane Home. Many of these cases were observed by me and I have already described [3] the biologic and serologic reactions of influenza bacilli producing meningitis. It seemed advisable to report the twenty-three cases, review the literature and try to correlate the available facts about this disease which has caused so much discussion since its recognition.

The cases reported in this paper are summarized in Table 2.

Table 3 contains a list of most of the authentic cases of influenzal meningitis on record. A number of such tables have been prepared by various workers. So many mistakes, however, were found in them that the original references have been consulted in nearly every instance. In that way the personal equation entering into the table has been limited to one person. Only infections of the meninges by *B. influenzae* alone are included in this series. When there is some doubt about the authenticity of the case, yet not enough to exclude it entirely, the fact is indicated.

Two hundred and twenty cases have been reported with seventeen recoveries (Tables 4, 5 and 6). The ages of 193 patients were given. Of these, 152 were under 2 years of age, forty-one were 2 years or older. Twelve of the seventeen recoveries, however, occurred in patients 2 years of age or older (Tables 5 and 6).

* Received for publication, March 30, 1922.

* From the Departments of Pathology and Bacteriology, and Pediatrics, Johns Hopkins University.

TABLE 2.—Summary of Twenty-Three Cases of Influenzal Meningitis

No.	Name	Date	Age, Mos.	Spinal Fluid	Blood Culture	Leukocytes	Differential Count	Duration, Days	Primary or Secondary	Outcome	Necropsy
1	R. T.	Oct., 1913	4	B. influenzae	Negative	13,760	—	13	Primary; ears normal 3 days before death	Died	Meningitis, internal hydrocephalus; otitis; arthritis; lungs normal
2	R. C.	Nov., 1914	14	B. influenzae	Negative	22,600	—	17	Primary; ears normal on admission	Died	Meningitis; acute bronchopneumonia; otitis; mastoiditis
3	W. K.	Dec., 1915	18	B. influenzae	Negative	76,500	—	35	Primary.....	Died	Meningitis; ethmoiditis; otitis; bronchopneumonia
4	C. L.	Oct., 1916	14	B. influenzae	—	25,750	—	9	Primary.....	Died	No necropsy
5	C. M.	July, 1917	11	B. influenzae	Negative	17,600	—	23	Primary; lungs and ears clear on admission	Died	No necropsy
6	H. S.	Oct., 1917	8	B. influenzae	Negative	14,000	—	15	Secondary, possibly to pneumonia; lumbar puncture done for meningismus; diagnosis accidental	Died	Meningitis; hydrocephalus; old and new bronchopneumonia; blood culture Type IV pneumococcus
7	E. M.	Dec., 1917	7	B. influenzae	Negative	13,800	—	13	Primary.....	Died	Meningitis, cloudy swelling of liver; other organs negative
8	G. J.	Feb., 1918	2½	B. influenzae	—	42,500	—	9	Primary.....	Died	Meningitis; bronchopneumonia; cloudy swelling of kidneys; blood culture Type II pneumococcus
9	L. R.	Aug., 1918	7	B. influenzae	—	32,000	—	49	Secondary, possibly to a cold and pneumonia	Died	Meningitis; hydrocephalus; brain abscess; old and new bronchopneumonia
10	C. L.	Dec., 1918	9	B. influenzae	—	21,200	P.M.N. 82%	13	Primary; Roentgen ray Ex. Dec. 3, lungs clear; Dec. 9, pneumonia right upper lobe; diagnosis accidental	Died	Meningitis; bronchopneumonia; peritonitis; B. influenzae from brain, lungs, peritoneum; blood culture, Staphylococcus aureus
11	A. P.	Dec., 1918	16	B. influenzae	Negative	27,500	P.M.N. 87%	24	Secondary, possibly to diphtheria	Died	No necropsy
12	H. M.	Jan., 1919	7	B. influenzae	Negative	50,880	P.M.N. 80%	26	Primary.....	Died	No necropsy
13	M. H.	Jan., 1919	3	B. influenzae	B. influenzae	20,400	—	33	Primary.....	Died	Meningitis; internal hydrocephalus; sinuses, ears and mastoids clear; blood culture, sterile
14	E. L.	Apr., 1919	7	B. influenzae	B. influenzae	28,000	—	13	Primary.....	Died	Meningitis; communicating hydrocephalus; cloudy swelling of kidneys; ears, sinuses, lungs clear
15	E. T.	Aug., 1919	17	B. influenzae	Negative	20,000	—	22	Secondary, possibly to a cold and mastoiditis	Died	Meningitis; slight recent bronchopneumonia
16	M. M.	Oct., 1919	12	B. influenzae	—	16,000	—	21	Primary; ears normal Roentgen ray Ex. of chest showed lungs normal	Died	No necropsy
17	M. S.	Nov., 1919	15	B. influenzae	B. influenzae	18,400	P.M.N. 63%	8	Secondary, possibly to cold and pneumonia	Died	Meningitis; bronchopneumonia
18	H. G.	Nov., 1919	13	B. influenzae	B. influenzae	12,200	—	—	Primary; lungs and ears clear	Recovered deaf	
19	S. D.	Jan., 1920	24	B. influenzae	B. influenzae	20,800	P.M.N. 77%	24	Primary; lungs and ears clear	Died	No necropsy
20	W. C.	Jan., 1920	8	B. influenzae	B. influenzae	21,600	P.M.N. 66%	29	Secondary, possibly to a cold and pneumonia	Died	No necropsy (developed arthritis before death)
21	M. E.	Nov., 1920	12	B. influenzae	B. influenzae	11,200	—	2	Primary; lungs and ears clear	Died	No necropsy
22	W. S.	June, 1921	10	B. influenzae	Negative	18,500	—	27	Primary; lungs and ears clear	Died	No necropsy
23	V. C.	Nov., 1921	10	B. influenzae	B. influenzae	28,300	P.M.N. 84%	12	Primary; Roentgen ray Ex. of chest showed lungs normal	Died	No necropsy

TABLE 3.—Authentic Cases of Influenzal Meningitis

Authority	No. Cases	Year Reported	Remarks	Authority	No. Cases	Year Reported	Remarks
Fraenkel[4]	2	1898		Henry[45]	7	1912-13	
Slawyk[5]	1	1899		Giese[46]	1	1913	
Meunier[6]	1	1900		Drucot[47]	1	1913	Probable case
Trailescu[7]	1	1901		Grasty[48]	1	1913	
Langer[8]	1	1901	Recovery	Ross and Moore[49]	1	1913	
Dubois[9]	1	1902		Spillman and Beneech[50]	1	1913	Probable case, recovery
Ghon[10]	1	1902		Wollstein[51]	3	1913	
Cagnetto[11]	2	1903-04		Atkinson[52]	1	1914	
Costinesco[12]	3	1903		Tebbutt[53]	1	1914	
Mya[13]	3	1903	1 recovery*	Nyberg[54]	2	1915	
Mya[14]	1	1903		Ely and Weingart[55]	1	1915	
Thomesco and Grascoski[15]	1	1904	Recovery	Imperatori[56]	1	1915	
Jundell[16]	2	1904	1 probable case	Cleland and Ferguson[57]	2	1915	
Bertini[17]	1	1904		Brown[58]	2	1915	
Cattaneo[18]	1	1905		Boland[59]	1	1915	
Simon[19]	1	1905	†	Hill and Packard[60]	5	1915	1 recovery
Dudgeon and Adams[20]	1	1907		Aaser[61]	1	1916	
Sprigg[21]	1	1907		Packard[62]	1	1916	Recovery
Douglas[22]	1	1907		Moody[63]	2	1916	2 probable cases
Saathoff[23]	1	1907		Williams[64]	1	1916	
Adams[24]	1	1907		Torrey[65]	2	1916	1 recovery
Bentz and Frye[25]	1	1908		Bhat[66]	1	1917	
McDonald[26]	1	1908	Probable case	Tobler[67]	1	1917	
Hymanson[27]	2	1909		Lacy[68]	2	1918	
Cohen[28]	3	1909		Hills[69]	1	1918	
Cohoe[29]	1	1909	Recovery	Albert and Kelman[70]	1	1919	§
Davis[30]	2	1909	1 probable case	Johnson[71]	1	1919	Recovery
Simon and Aine[31]	5	1910		Dunn[72]	10	1920	‡
Simon[32]	2	1910		Stone[73]	1	1920	Recovery
Batten[33]	5	1910	1 recovery	Litchfield[74]	1	1920	Recovery
Ager and Avery[34]	1	1910		Christiansen and Kristensen[75]	3	1921	1 recovery
Ritchie[35]	3	1910	1 probable case	Finkelstein[76]	1	1921	
Sayce[36]	7	1911	1 recovery	Abt[77]	1	1921	
Clemens and Gould[37]	1	1911		Koplik	9	1921	§
Dunn[1]	4	1911		Neal[2]	32	1921	1 recovery
Rhea[38]	2	1911		Neal	3	1921	§
Prasek and Zattelli[39]	1	1911		Davis	2	1921	§
Wollstein[40]	7	1911		Ill.	1	1922	§
Brem and Zeiler[43]	2	1911		Rivers	23	1922	1 recovery
Davis[42]	5	1911					
Jundell[43]	1	1912					
Klinger[44]	4	1912	1 recovery				
Total					220		17 recoveries

* One of these cases also reported by Caccia.
† Reported also in 1902 and counted twice by Simon in 1910.
‡ Eleven reported, but one included under Wollstein in 1913.
§ Personal communication.

TABLE 4.—Mortality Rate

Authority	Number Cases	Number Recovered	Mortality, per Cent.
Rivers	23	1	96
Neal	35	1	97
All others	162	15	91
Total	220	17	92

TABLE 5.—Relation of Age to Incidence and to Death or Recovery in One Hundred and Ninety-Three Cases in Which Age Was Stated

Age	Number Cases	Number Deaths	Number Recoveries	Age Incidence, per Cent.	Mortality, per Cent.
Under 2 years	152	147	5	79	97
2 years and older	41	29	12	21	71

TABLE 6.—List of Recoveries *

No.	Authority	Date Reported	Age of Patient	Duration in Days	Sequels
1	Langer[8]	1901	9 yrs.		
2	Mya[13]	1903	9 mos.	49	Residual left facial paralysis, residual left hemiplegia
3	Thomesco and Grascoski[15]	1904	7 yrs.	10	
4	Cohoe[29]	1909	33 yrs.	15	
5	Batten[33]	1910	14 mos.	30	Partial blindness, difficulty in sitting and walking
6	Sayce[36]	1911	4 yrs.		
7	Klinger[44]	1912	26 yrs.	60	
8	Spillman and Benech[50]	1913	Adv. age	14	
9	Hill and Packard[60]	1915	4 mos.	20	
10	Packard[62]	1916	11 yrs.	17	
11	Torrey[65]	1916	11 yrs.	20	
12	Johnson[71]	1919	3 yrs.		
13	Stone[73]	1920	15 yrs.	11	Double optic neuritis with some residual blindness; some residual involvement of third nerve on one side
14	Litchfield[74]	1920	23 mos.	70	
15	Christiansen and Kristensen[75]	1921	2 yrs.	23	
16	Neal[2]	1921	2½ yrs.	30	
17	Rivers	1922	13 mos.	..	Complete nerve deafness

* Twelve of seventeen recoveries, 71 per cent., occurred in patients 2 years of age or older.

CLINICAL PICTURE

The diagnosis of meningitis of all kinds is difficult in infants and young children. Influenzal meningitis is no exception. The 220 cases on record must be only a few of those diagnosed, and the number recognized does not necessarily include all that actually occurred. Batten [33] agrees with me that many are overlooked.

There is no group of clinical findings peculiar to influenzal meningitis. At times it is indistinguishable clinically from epidemic cerebrospinal meningitis. A hemorrhagic rash [2] even may be present which is supposed to be characteristic of the latter disease. It may simulate tuberculous meningitis, as an extreme bulging of the fontanel, paralysis of the eye muscles and irregular respirations (atypical Cheyne-Stokes) are frequently seen in patients living many days. Henry [45] reported the spontaneous rupture of the fontanel in an infant 10 months of age. A strabismus was seen at some time in ten of my twenty-three patients. Paralysis of the face or extremities, arthritis, deafness and blindness occur in the order mentioned. The temperature may be elevated continuously or irregularly. Febrile periods may alternate with periods of

normal temperature (see temperature charts accompanying the abstracts of case records). Influenzal meningitis is most commonly mistaken for pneumonia and this is probably due to an unexplained fever associated with rapid, difficult or embarrassed respirations.

White Blood Cell Count.—A leukocytosis with an increase in the percentage of the polymorphonuclear cells is usual (Table 7). Influenzal meningitis, a pure infection with Pfeiffer's bacillus, has an entirely different blood picture from the one seen in epidemic influenza which is accompanied by a leukopenia.

TABLE 7.—WHITE BLOOD CELL COUNT IN INFLUENZAL MENINGITIS

	White Blood Cells per C. Mm.				Per Cent. Polymorphonuclear Cells	
Authority	No. Cases	Low	High	Average	No. Cases	Average
Rivers	23	11,200	76,500	24,499	7	77
All others	17	7,600	38,000	17,018	10	78
Total	40	7,600	76,500	21,320	17	78

The figures show that a polymorphonuclear leukocytosis is usually present in influenzal meningitis.

Blood Cultures.—In eighteen of my cases records of antemortem blood cultures are available (Table 2). Eight, or 44 per cent., were positive for *B. influenzae*. Most of the positive results were obtained from the patients listed in the last half of the table. So many negative results in the first half may have been due to inability to grow the bacilli when present. Records of antemortem and postmortem blood cultures were found in twenty-four instances in the review of the literature. Sixteen were positive for influenza bacilli.

Spinal Fluid.—Early in the disease the spinal fluid is slightly turbid with a ground-glass appearance. Usually polymorphonuclear cells predominate. Later the fluid may become so purulent and thick that it often flows with great difficulty or not at all through the needle. Batten [33] believes that a very purulent fluid is more or less indicative of influenzal meningitis. Smears of the fluid practically always show many gram-negative pleomorphic bacilli, usually extracellular. No difficulty should be experienced in obtaining cultures of these bacilli when the proper medium is used.[78] An indole test on the spinal fluid, as described by Rivers,[79] is an aid in rapid diagnosis. While the bacilli are easily demonstrated in direct smears or in cultures by one accustomed to working with them, they may be overlooked by one less experienced. Consequently, some cases of influenzal meningitis may be treated as meningococcus infections in which no organisms were seen or grown and tabulated as deaths from epidemic cerebrospinal meningitis.

Duration.—A false impression of the duration of the disease may be obtained from a few cases. Death may come quickly, in from twenty-four to thirty-six hours, or the patient may linger for days or months. Sayce [36] reported that a child, 5 years old, lived six months after the diagnosis of influenzal meningitis had been established. Eighteen lumbar punctures were made at various times and *B. influenzae* was isolated. At the necropsy these findings were confirmed. Many patients lived twenty, thirty, forty or sixty days. The average duration of the disease in thirty-two of Neal's patients was sixteen days; in Rivers' twenty-two cases, twenty days; in 112 cases, all others, eighteen days. The average for these three groups, comprising 166 patients, was eighteen days. The duration of the disease in the patients who recovered was given in thirteen instances (Table 6). The average was twenty-eight days.

Sequels.—Four of the seventeen recoveries were not complete (Table 6). Blindness, paralyses and deafness are the usual sequels.

NECROPSIES

The pathologic findings at necropsy depend a great deal on the duration of the disease before death. This is well illustrated by Rhea's [38] two cases. The first patient was an infant 6 months old which died after an illness of three days. The necropsy revealed an acute hemorrhagic meningitis and encephalitis, an acute pharyngitis, laryngitis and bronchopneumonia. The heart's blood was sterile. A pure culture of influenza bacillus was obtained from the meninges and the bacilli were also seen in the exudate in the sections of the meninges. The encephalitis may explain some of the paralyses reported. The second patient was a child 5 years of age which became sick suddenly. Influenza bacilli were obtained in pure culture from the spinal fluid and the blood. Before death, which came after an illness of eighty-nine days, a left hemiplegia and signs of hydrocephalus developed. An organizing meningitis with thickening and thrombosis of many of the blood vessels, and an internal hydrocephalus were found at necropsy. The ears, sinuses and lungs were normal. Cultures from the meninges and heart's blood remained sterile. These two cases are probably the extremes of the pathologic picture, which is usually one of a massive purulent meningitis. The exudate may collect at the base, along the vessels or in patches over the cortex. At times, the whole brain seems to be wrapped in a layer of pus 2 mm. thick. Hydrocephalus is common. A brain abscess has been observed twice (Davis; [42] Rivers). Bronchopneumonia is found in a large number of the patients. Otitis media, sinusitis, arthritis, peritonitis, nephritis and cloudy swelling of the liver and kidneys are some of the findings in other parts of the body.

ABSTRACTS OF CASE RECORDS

Abstracts of eight case records are given to illustrate many points already mentioned and to emphasize others that will be considered later.

CASE 1 (1).—R. T., colored boy, 4 months old, became ill Oct. 20, 1913, with a "pain in the stomach" and loose bowels. These symptoms increased somewhat in severity until October 28, when the mother noticed while bathing and dressing the child that the left shoulder was tender. There was no history of a cough, vomiting or convulsions. Drowsiness was noticed for the first time October 30, the day of admission to the hospital. The physical examination on admission showed a stiff neck, retracted head, hyperesthesia,

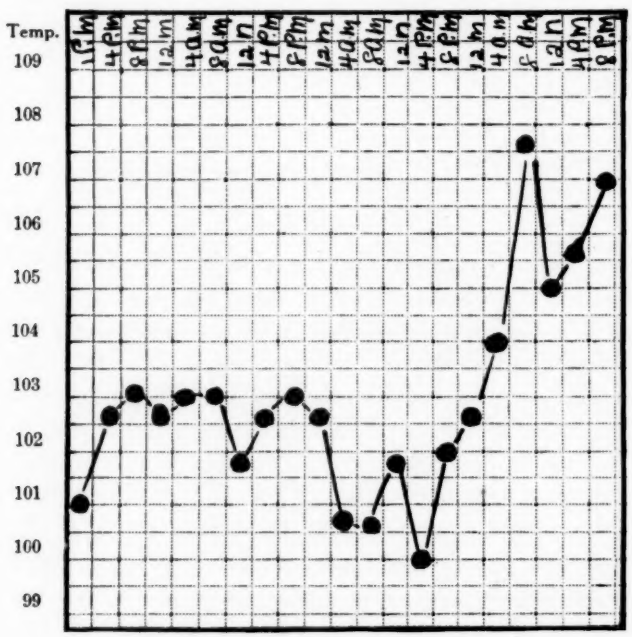

Fig. 1.—Temperature Chart for Case 1.

no discharge from the nose, normal ear drums, atypical Cheyne-Stokes respirations, normal lungs and heart, spastic paralysis of the left arm, no arthritis of the left shoulder or elbow, swelling of the left wrist and exaggerated deep reflexes. Kernig's sign was present. The white blood cell count was 13,760. The spinal fluid was cloudy. Gram-negative bacilli were seen in smears of the spinal fluid. Culturally these were influenza bacilli. The blood culture remained sterile. November 1 an internal strabismus of the right eye and a fluctuation in the swelling of the left wrist were noticed. A second blood culture made at this time also remained sterile. The patient died November 2, after an illness of thirteen days.

Anatomic Diagnosis (Necropsy 4015).—Fibropurulent cerebrospinal meningitis, internal hydrocephalus, suppurative otitis media (right), suppurative arthritis of left wrist, focal necrosis of liver, thrombosis of portal vein, pseudo-infarction of liver.

Remarks.—The intern obtained no history of a respiratory infection preceding the illness. Intestinal symptoms predominated at the onset. After the diagnosis of influenzal meningitis was made, however, the resident managed to secure from the mother some kind of an indefinite history of a "cold" from which the child had suffered. The temperature chart would pass for that of a patient with tuberculous meningitis. No portal of entry was found at necropsy unless it were the otitis media, but the ear drums were normal to otoscopic examination three days before death.

CASE 2 (5).—C. M., colored girl, 11 months old, refused to eat, had fever and held her head retracted, July 13, 1917. She would not use her right arm as before. Two days later the mother noticed a "cap" (bulging fontanel) on the baby's head. The patient was admitted to the hospital July 17.

The physical examination on admission showed a conscious, irritable, hyperesthetic, rachitic child with a stiff neck and bulging fontanel, an internal

Fig. 2.—Photograph showing the bulging fontanel in Case 5.

strabismus of the left eye, no discharge from the nose, normal ear drums, and no definite signs of pneumonia. Kernig's sign was absent. The right arm was used less than the left. The white blood cell count was 17,600. A tentative diagnosis of tuberculous meningitis was made. The spinal fluid was slightly turbid with a cell count of 750 per c. mm. About half of the cells were mononuclears. Films formed but no tubercle bacilli were found. Other organisms were not looked for or were missed. Cultures were not made at this time. July 31 another lumbar puncture was made to search for tubercle bacilli. At this time gram-negative bacilli were seen and properly identified as *B. influenzae*. Another examination of the spinal fluid, August 3, confirmed the diagnosis of influenzal meningitis. A blood culture made August 1 remained sterile. The respirations became irregular, atypical Cheyne-Stokes. Definite signs of pneumonia developed before death, which occurred August 5. A necropsy was not allowed.

Remarks.—This illustrates how easily influenzal meningitis can be mistaken for tuberculous meningitis. From the history and the course in the hospital nothing to which the meningitis could have been secondary was found. The pneumonia developed after the patient came into the hospital.

Case 3 (7).—E. M., white girl, 7 months old, refused to nurse Dec. 8, 1917. She remained in a stupor for twenty-four hours, after which she began to have convulsions. These convulsions, five or six a day, involved only the right side of the body and persisted until admission to the hospital, December 17. The mother noticed that the head was retracted December 16.

The physical examination on admission showed a retracted head, no discharge from the nose, slightly reddened ear drums, normal lungs, and constant twitchings of the right arm and leg. Kernig's sign was present. White blood cell count was 13,800. The spinal fluid was cloudy and contained gram-negative bacilli which were influenza bacilli culturally. The blood culture remained sterile. Roentgen-ray examination of the lungs on the day of admission showed that they were practically normal. Temperature ranged between 101 and 103 F. most of the time, but dropped nearly to normal before death, December 21.

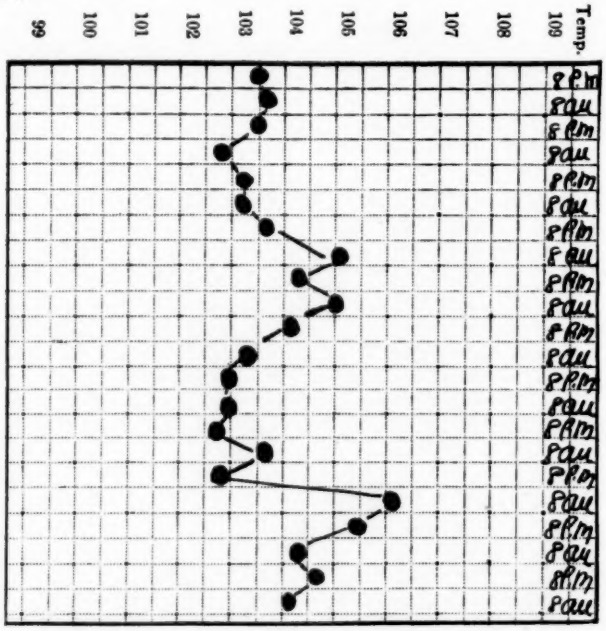

Fig. 3.—Temperature Chart for Case 5.

Anatomic Diagnosis (Necropsy 5396). — Purulent cerebrospinal meningitis, cloudy swelling of the liver.

Remarks.—There is nothing in the history, physical examination, course in the hospital, or in the necropsy findings to suggest that this was anything other than a primary influenzal meningitis.

Case 4 (8).—G. J., colored girl, 2½ months old, became drowsy, refused to nurse and "rolled eyes up," Feb. 26, 1918. She gradually became worse and would scream when touched. March 4 the child began to have convulsions and was admitted to the hospital the next day.

The physical examination on admission showed a bulging fontanel, retracted head, stiff neck, internal strabismus of the left eye, no discharge from the nose or ears, few râles in the lungs. palpable spleen and exaggerated deep reflexes. Kernig's sign was present. White blood cell count was 42,500. The

spinal fluid was cloudy and contained gram-negative bacilli which culturally were influenza bacilli. Patient died March 7.

Anatomic Diagnosis (Necropsy 5473).—Massive purulent cerebrospinal meningitis, acute splenic tumor, cloudy swelling of the kidneys, bronchopneumonia, fibrous pleural adhesions (bilateral).

Necropsy Bacteriology.—Culture from meninges showed only *B. influenzae.* Culture from heart's blood showed only pneumococcus Type II.

Remarks.—The patient was afebrile while in the hospital. As far as can be determined, this is an example of a primary influenzal meningitis. Only small areas of bronchopneumonia were found in the lungs. The Type II pneumococcus found in the blood at the necropsy is interesting. Fixed types of pneumococci usually produce lobar pneumonia. They can, however, under the proper conditions act as secondary invaders and even cause bronchopneumonia.

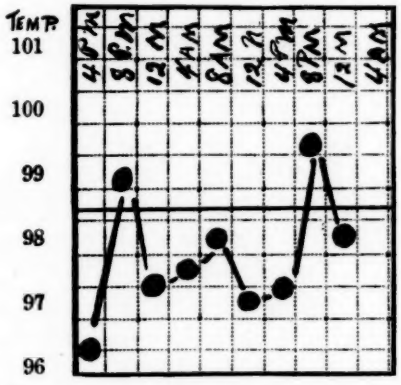

Fig. 4.—Temperature Chart for Case 8.

CASE 5 (12).—H. M., white female, 7 months old, became drowsy and feverish three weeks before admission to the hospital. At first there was a slight discharge from the nose. The family physician treated the baby for bronchitis in spite of the fact that she had no signs of it, not even a cough until a few days before coming to the hospital. One week before admission projectile vomiting after each feeding developed and three days before admission the head became retracted. The patient was admitted Jan. 21, 1919.

The physical examination showed a conscious, hyperesthetic baby with a stiff neck and a retracted head, no discharge from the nose or ears, anisocoria, indefinite signs of pneumonia in right interscapular region, exaggerated deep reflexes. White blood cell count was 50,880. The spinal fluid was very thick and purulent. Gram-negative bacilli were seen in the smears. Culturally, these were influenza bacilli. The blood culture remained sterile. The child gradually became worse and began to have numerous convulsions before she died January 26. A necropsy was not allowed.

Remarks.—The child probably had a meningitis from the beginning. It was primary as far as can be determined. In spite of a purulent meningitis the temperature was normal for two days after admission to the hospital. The rise in temperature several days before death cannot be accounted for definitely. There are two possibilities, a

terminal rise before death that is seen not infrequently in meningitis, or the development of a pneumonia.

CASE 6 (14).—E. L., white boy, 7 months old, became irritable April 4, 1919. He gradually grew worse and would scream when touched or handled. Stiffness of his neck was noticed April 8, two days before admission to the hospital.

Physical examination when first seen showed a conscious child with a bulging fontanel, retracted head and stiff neck, no discharge from the nose, normal ear drums, normal lungs, and paralysis of the right arm. Kernig's sign was absent. White blood cell count was 28,000. The spinal fluid was cloudy. Gram-negative bacilli were seen in the smears. Culturally these were influenza bacilli. From the blood culture influenza bacilli were obtained also. April 10 it was noticed that the paralysis of the right arm had disappeared. The child gradually became worse. Before death, which occurred April 17, convulsions set in and an external strabismus of the right eye was seen.

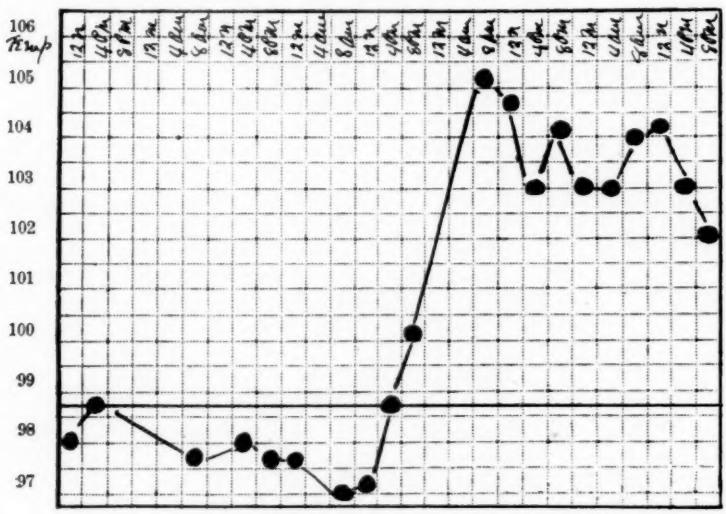

Fig. 5.—Temperature Chart for Case 12.

Anatomic Diagnosis (Necropsy 5880).—Purulent cerebrospinal meningitis, communicating hydrocephalus, cloudy swelling of the kidneys.

Remarks.—The ears, sinuses and lungs were normal while in the hospital and at necropsy. Influenza bacilli were obtained from the spinal fluid and blood during life and from the meninges and heart's blood at necropsy. The bacilli were pathogenic for rabbits.

CASE 7 (18).—H. G., white girl, 13 months old, became irritable and "droopy" Nov. 24, 1919. No history of vomiting, convulsions or rigidity was obtained. An internal strabismus of the left eye appeared November 26, the day before the patient was brought to the hospital.

Physical examination showed a conscious, irritable, restless child that would not sit or stand as formerly, tense fontanel, internal strabismus of left eye, no discharge from the nose, normal ear drums, normal lungs. Kernig's sign absent. White blood cell count was 12,200. The spinal fluid was cloudy. Gram-negative bacilli were found in the smears. The organisms were

B. influenzae culturally. Influenza bacilli were obtained from the blood culture. The patient was taken home November 28. The child was a private patient of Dr. Hamburger. He reported later that she had recovered but was completely deaf.

Remarks.—There is nothing in the history, physical examination, or course of the disease to obviate the possibility that this might have been a primary influenzal meningitis. The organism was pathogenic for rabbits.

CASE 8 (19).—S. D., white girl, 2 years old, suddenly developed fever and irritability Jan. 13, 1920. Three days later the neck became stiff. An internal strabismus of the left eye was noted January 18, the day of admission to the hospital.

Physical examination on admission showed a conscious child that would answer questions, but had a stiff neck, internal strabismus of the left eye, no discharge from the nose, normal ear drums, normal lungs. Kernig's sign was present. White blood cell count was 20,800. The spinal fluid was cloudy.

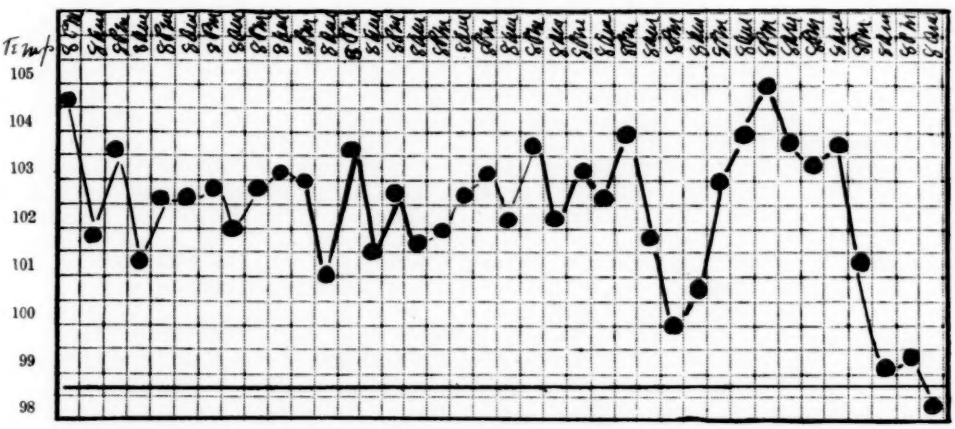

Fig. 6.—Temperature Chart for Case 19.

Gram-negative bacilli were seen in the smears. The organisms were *B. influenzae* culturally. Influenza bacilli were obtained from the blood culture. During the first twelve days in the hospital the patient did not seem very sick. She would eat, move around the bed and talk. Then she began gradually to become more ill until she died February 6. The spinal fluid became so thick toward the last that it would not run through the needle. No signs of pneumonia were made out at any time. Six days before death the right ear drum became inflamed. A necropsy was not allowed.

Remarks.—This is another example, as far as can be determined, of a primary influenzal meningitis. The right ear drum became inflamed eleven days after the patient came to the hospital, about the time she became much worse and when under less favorable conditions the meningitis might have been recognized for the first time. No doubt many infections of the middle ear reported in connection with influenzal meningitis and thought of as possible portals of entry have occurred late in the course of an unrecognized meningitis.

This clinical picture is well known. Nothing further can be gained by reporting cases as they occur. The main interest is centered around the question of whether influenzal meningitis is a primary or a secondary disease. No attempt will be made to tabulate all the ideas on the subject expressed by various workers. It seems they can be divided into three main groups. Under each of these will be given a few specific references.

DIFFERENT CONCEPTIONS REGARDING NATURE OF INFLUENZAL MENINGITIS

1. *Secondary to a Respiratory Infection.*—Many clinicians thought and still believe that *B. influenzae* is the cause of epidemic influenza. Naturally these observers would conclude that influenzal meningitis is a complication of a respiratory infection. Wollstein [40] and Dunn [72] are of that opinion. Flexner [80] said, "It is probable that the infection of the meninges is always secondary to the respiratory infection." Hill and Packard [60] stated that the portal of entry was through the respiratory tract, secondary to influenza.

2. *Part of a Generalized Infection.*—Dudgeon and Adams [20] considered the meningitis a part of a metastatic pyemic condition. Cohen [28] also thought that the meningitis was a part of a generalized infection. He believed, however, that this infection was caused by a definite group of organisms which he claimed differed from Pfeiffer's bacillus and called them *Bacille méningite cérébrospinale septicémique.*

3. *A Primary Meningitis.*—Klinger [44] hinted that influenzal meningitis might be a primary idiopathic disease similar to epidemic cerebrospinal meningitis and was so bold as to suggest that the patients be isolated and that some kind of disinfection be observed in connection with them. Nyberg [54] thought that one of his patients had a primary influenzal meningitis caused by one of a group of influenza bacilli having a predilection for the meninges.

The pathogenesis of influenzal meningitis will not be discussed in this paper further than to state that one's ideas in regard to it might vary, depending on whether it proves to be a primary or a secondary disease. Consequently all the evidence possible has been collected to determine whether any definite conclusions about the latter question can be reached.

INFORMATION FROM HISTORIES AND NECROPSIES

Histories.—The records of cases of influenzal meningitis reported in the literature and of the twenty-three cases in my series have been analyzed to discover what evidence they may provide as to the primary or secondary nature of the disease. With the exception of Neal's [2] thirty-two cases, my judgment is a large factor in Tables 8 and 9.

Observers reporting cases have gone out of the way to find some preceding infection to which the meningitis might have been secondary. This is well illustrated by Case 1 in my series. In certain instances it is fairly evident that the meningitis was overlooked for a long time, often until after an otitis media, an arthritis, or a pneumonia had been found. In some instances, the minority, however, the meningeal infection was undoubtedly secondary, particularly to mastoiditis. Three of Henry's [45] patients who were operated on for acute mastoid infections are good examples. Unfortunately, two of them have to be omitted as the meningitis was caused by two organisms—hemolytic streptococci and influenza bacilli. Other examples of secondary infections have been reported by Packard [62] and Imperatori.[56] In 171 instances (Table 8) it was possible from the history and course of the disease to form some opinion as to whether the meningitis was primary or secondary.

TABLE 8.—Division of One Hundred and Seventy-One Cases, from Their Histories, Into Possible Primary and Possible Secondary Infections

Authority	Number Cases	Number Primary	Number Secondary	Per Cent. Primary	Per Cent. Secondary
Rivers	23	17	6	74	26
Neal	32	24	8	75	25
All others	116	86	30	74	26
Totals	171	127	44	74	26

Necropsies.—Bronchopneumonia was found in the majority of the cases at necropsy. Immediately the question arises as to whether the pneumonia was complicating the meningitis or vice versa. Bertini [17] and Davis [42] state that they could not be certain whether the pneumonia antedated the meningitis in their cases or not. Giese,[46] in reporting a case of influenzal meningitis, said that the meningitis was primary and that the slight pneumonia present was secondary. Torrey [65] and Tobler [67] suggested that the influenza bacilli pass from the cerebrospinal space into the circulation, giving rise to secondary infections in other organs. It is also possible that some of the pneumonia in these cases is caused by pneumococci or streptococci, similar to that occurring in children with dysentery or severe diarrheas. Christiansen and Kristensen [75] reported that they recovered from the meninges of a patient dead of influenzal meningitis a pure culture of influenza bacilli and from the pneumonic consolidation in the lungs a pure culture of pneumococci. From two of my patients (Nos. 6 and 8) evidence was obtained that other bacteria might cause some of the complications found at necropsy. These patients had bronchopneumonia in addition to a meningitis. A pure culture of influenza bacilli was obtained from the meninges of both cases, while from the heart's blood of one case

a pure culture of a Type IV pneumococcus was recovered and from the heart's blood of the other a pure culture of a Type II pneumococcus was recovered. Unfortunately, cultures from the lungs were not made or the results were not recorded.

Necropsies were obtained in twelve of the twenty-two fatal cases in my series. In three of these twelve, 25 per cent., meningitis alone was found. The ears, sinuses, and lungs were normal. If there was a primary focus, it was overlooked or it had healed. The patients had been sick eleven, thirteen and thirty-three days, respectively. From the literature records of seventy-one necropsies, many of which were partial, have been examined. Often the findings in the brain were given without stating whether the other organs were normal or not examined. In spite of these difficulties, however, records of ten cases were seen in which a meningitis alone was found. The number of possible primary

TABLE 9.—THE NUMBER OF POSSIBLE PRIMARY CASES OF INFLUENZAL MENINGITIS AS DETERMINED BY SEVENTY-ONE NECROPSY RECORDS

No. Cases	Necropsy Findings	Per Cent.
10	Meningitis alone	14
1	Meningitis, peritoneal fluid contained B. influenzae, blood culture sterile, lungs, ears, and sinuses normal	
1	Meningitis, peritonitis (B. influenzae), blood culture sterile, lungs normal	
3	Meningitis, lungs normal	
2	Meningitis, lungs and ears normal	27
3	Meningitis, otitis media	
1	Meningitis, pericarditis, endocarditis	
2	Meningitis, arthritis	
1	Meningitis, bronchopneumonia (pure culture pneumococcus)	
5	Meningitis, small patches of bronchopneumonia which in some instances was suggested as being secondary	
29	Total possible primary cases	41

cases of influenzal meningitis observed at necropsy are listed in Table 9. If these figures are correct, it would be easy to assume that many more were primary also, the pneumonia and other pathologic lesions complicating the meningitis.

Possibility of Spread by Carriers.—So few cases of influenzal meningitis occur that it is impossible to show that the disease is spread by contact. There are facts, however, that might make one think that it is spread by carriers. Many observers report several cases occurring within a short time of each other. Hill and Packard [60] saw four cases in six months. Henry [45] observed at least five cases in 1910. In Dr. Howland's clinic seven cases were seen in one year. Simon and Aine,[31] in reporting five cases, speak of them as a little epidemic of influenzal meningitis. Davis [30] reported that twins 5 days old became ill at the same time, one died on the ninth day, the other on the twelfth. At the necropsy the first one was found to have had an influenzal meningitis. No lumbar puncture or necropsy was made in the second case.

Although there may be some doubt about the second child having a meningitis, yet it is reasonable to suppose that it did, as it became ill at the same time and ran a course similar to the other. Davis [42] also reported two cases of influenzal meningitis that occurred in a small institution of about fourteen inmates. The second child became ill two weeks after the death of the first. While not convincing, the evidence is at least suggestive that influenzal meningitis is a carrier-borne disease.

Incubation Period.—Enough information is not available to draw any conclusions in regard to the length of the incubation period. In the case of Davis' twins, however, one can be certain that the incubation period was not longer than five days.

Yearly Incidence of Influenzal Meningitis.—Jordan [81] and Neal [2] have commented on the fact that there was no great increase in influ-

TABLE 10.—YEARLY INCIDENCE OF TWO HUNDRED AND THREE CASES OF INFLUENZAL MENINGITIS

Year	Number of Cases			Year	Number of Cases		
	Year Stated	Year Approximated	Total		Year Stated	Year Approximated	Total
1897	2	0	2	1910	21	6	27
1898	0	0	0	1911	6	2	8
1899	2	1	3	1912	9	2	11
1900	0	0	0	1913	5	2	7
1901	0	2	2	1914	9	0	9
1902	8	3	11	1915	11	4	15
1903	2	3	5	1916	9	0	9
1904	0	0	0	1917	12	0	12
1905	1	1	2	1918	12	0	12
1906	3	0	3	1919	18	0	18
1907	10	0	10	1920	10	0	10
1908	8	0	8	1921	6	0	6
1909	6	7	13				
Total					170	33	203

enzal meningitis during and after the pandemic of influenza in 1918. This was used to show that there is no definite relationship between the etiology of the two diseases. Table 10 and Figure 7 give the incidence of influenzal meningitis by years in 203 instances where the year was stated or could be approximated.

Regardless of the etiology of epidemic influenza it would be difficult for one to deny an increased prevalence of *B. influenzae* during the last pandemic of that disease. With this increased prevalence of influenza bacilli and with so much disease of the respiratory tract there should have been a decided increase in the number of cases of influenzal meningitis if the ordinary respiratory strains of *B. influenzae* were the usual cause of the latter disease. From Table 10 and Figure 7 it is evident that there was no marked general rise in the number of cases. In Chicago, according to Jordan [81] and Davis,[82] there was practically no influenzal meningitis. In New York, according to Neal,[2] only one

case occurred during the epidemic of influenza in the autumn of 1918. There was, however, a slight rise in the number of cases for 1916, 1917, 1918 and 1919. In Baltimore, on the other hand, there was a decided increase during 1917, 1918, 1919 and 1920 (Fig. 7). In spite of this increase in the number of cases, no definite relationship between

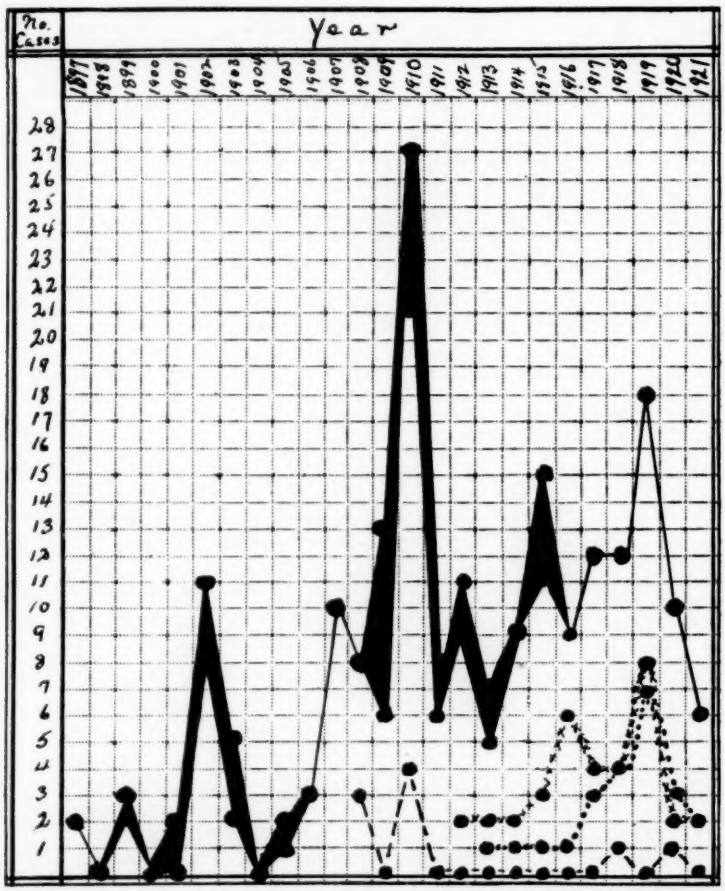

Fig. 7.—The unbroken line shows the yearly incidence of 203 cases of influenzal meningitis. The lower level of the shaded areas represents the number of cases that were stated as occurring in that year, the upper level represents the above cases plus the ones in which the year of occurrence was approximated. ————, yearly incidence in Chicago of cases seen by Davis; ....., yearly incidence of Rivers' cases in Baltimore; x x x x, yearly incidence of Neal's cases in New York City.

influenza and influenzal meningitis can be discovered as the majority of the cases of the latter disease did not occur during the epidemics of the former. All one can say is that in different localities there is a fluctuation in the number of cases of influenzal meningitis from year to year and that this fluctuation is not dependent on epidemic influenza.

The year of occurrence can be approximately stated in 203 instances of influenzal meningitis (Table 10 and Fig. 7). The striking thing is that the greatest number in one year was in 1910 when the world was exceptionally free of epidemic and interepidemic influenza.[83] A possible explanation for this will be apparent when the biologic and the serologic reactions of the meningitic and respiratory strains of *B. influenzae* are compared.

Seasonal Incidence of Influenzal Meningitis.—The month of occurrence of the cases of influenzal meningitis was stated in 126 instances. Most of them were in October, November, December and January (Fig. 8). In Baltimore pneumonia is more prevalent after Christmas, while influenzal meningitis (Fig. 8) occurs more frequently during the months just before Christmas, prior to the pneumonia season. In New York the majority of Neal's [2] cases occurred also during the months of October, November, and December (Fig. 8). Holt [84] has pointed out that in New York the curve of tuberculous meningitis, plotted by months, follows the curve of deaths from pneumonia (Fig. 8). The peaks of these curves come well after Christmas, in March and April. The etiology of tuberculous meningitis cannot be confused with that of ordinary pneumonia. Holt suggested that the curves parallel each other because acute respiratory diseases cause an exacerbation and a dissemination of tuberculosis. On the other hand, the curve of influenzal meningitis, which has been considered by many to be secondary to acute respiratory infections, does not follow the curve of deaths from pneumonias as closely as does tuberculous meningitis (Fig. 8).

Biologic and Serologic Reactions of Different Influenza Bacilli.—If influenzal meningitis be a primary disease in most instances, one would expect to find a close relationship culturally and serologically between the strains producing it. Povitsky and Denny [85] demonstrated that four of seven meningitic strains were identical by absorption of agglutinin tests. Rivers and Kohn,[3] working with thirteen strains of influenza bacilli isolated from the meninges or the spinal fluids of patients with influenzal meningitis, showed that eleven were alike culturally. These eleven strains were closely allied, as shown by agglutination tests. By absorption of the agglutinin test two main groups were found: Group I of seven strains; Group II of three strains, an intermediate group of one strain. At that time four blood culture strains isolated from children with pneumonia following influenza were studied also. These were found to be different from each other and from the meningitic strains. Since the publication of that paper two more meningitic strains have been studied, one of which fell into Group I, the other was identical with none of the other strains. This grouping of the meningitic strains is especially marked in distinc-

tion to the apparent heterogeneity of the respiratory strains as shown by Valentine and Cooper,[86] Povitsky and Denny,[85] Chesney,[87] and others.

I have compared the meningitic strains with fourteen respiratory ones other than the four blood culture strains already mentioned. In no instance was any one of the respiratory strains identical with the meningitic strains serologically, even when they had similar cultural characteristics. If influenzal meningitis proves to be a carrier-borne

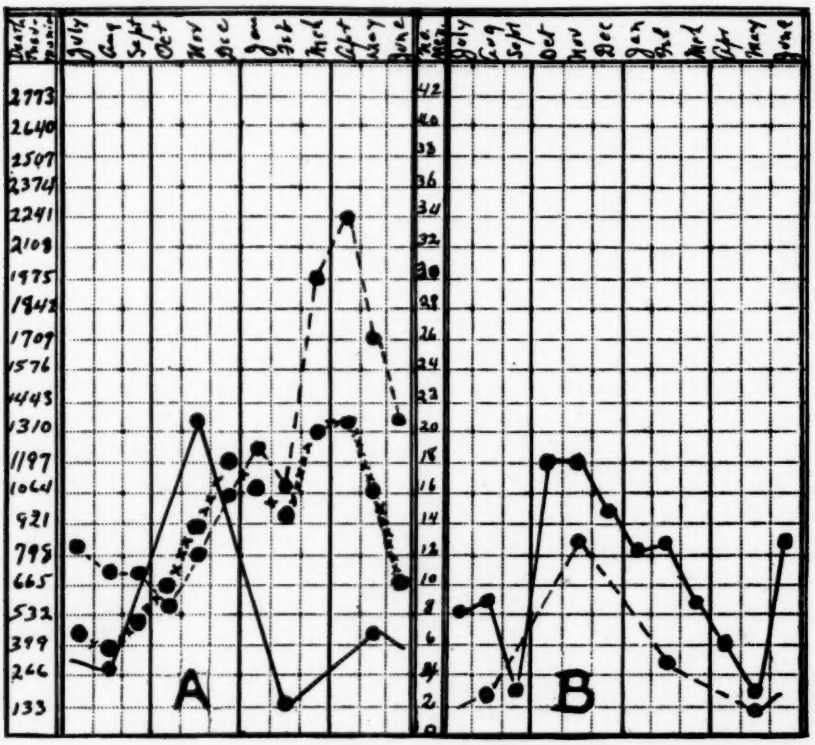

Fig. 8.—A. xxxx, seasonal incidence of deaths from pneumonia in New York City for one year. ————, seasonal incidence of 218 cases of tuberculous meningitis in New York City. ————, seasonal incidence of thirty-five cases of influenzal meningitis in New York City. The two upper curves were copied from Holt.[84] The lower curve was plotted from Neal's[2] figures.

B. ————, seasonal incidence of 126 cases of influenzal meningitis. ————, seasonal incidence of Rivers' twenty-three cases of influenzal meningitis.

disease, however, meningitic strains will be found eventually in throat cultures. In all, fifteen meningitic strains have been studied, eight of which were in Group I, three in Group II, one intermediate, and three heterogeneous strains. Of eighteen respiratory strains none was found identical with the meningitic strains. These results are summarized in Table 11.

From four of the patients with a meningitis blood culture strains were obtained and studied also. These were found to be identical with the corresponding meningeal strains. This is contrary to the findings of Anderson and Schultz,[88] who reported that the meningeal and the blood culture strains from the same patient were different immunologically.

The fact that most of the meningitic strains of *B. influenzae* are different from the respiratory ones probably accounts for the absence of a marked increase in the prevalence of influenzal meningitis during the pandemic of influenza when influenza bacilli were plentiful in diseased respiratory tracts.

Relative Pathogenicity of Meningeal and Respiratory Strains.—Cohen,[28] and Cohen and Fitzgerald [89] were among the first to suggest that *B. influenzae* from patients with meningitis differed from ordinary

TABLE 11.—SUMMARY OF THE BIOLOGIC AND THE SEROLOGIC REACTIONS OF FIFTEEN MENINGITIC AND EIGHTEEN RESPIRATORY STRAINS OF B. INFLUENZAE

	Biologic Reactions					Groups Determined by Absorption Tests		
No. Strains	Nitrate Reduction	Indol Formation	Glucose	Xylose	Maltose	Group I	Intermediate	Group II
Meningitic								
8	+	+	+	+	—	+	—	—
1	+	+	+	+	—	—	+	—
3	+	+	+	+	—	—	—	+
1	+	—	+	+	—	—	—	—
1	+	+	+	—	—	—	—	—
1	+	+	—	—	—	—	—	—
Respiratory								
7	+	+	+	+	—	—	—	—
4	+	+	+	—	—	—	—	—
5	+	—	+	+	—	—	—	—
1	+	—	+	+	+	—	—	—
1	+	—	+	—	+	—	—	—

+ indicates nitrates are reduced and indol is formed; — indicates the oppposite. Under the sugars + indicates acid is formed without gas; — indicates neither acid nor gas is formed. Under grouping + indicates into which group the strains fall; — indicates that the strains do not belong to that group.

respiratory influenza bacilli. They based their conclusions on results of agglutination tests, protection experiments, and on the fact that the meningitic strains were highly pathogenic for rabbits. Wollstein,[40] from her studies concluded that respiratory and meningeal strains of *B. influenzae* were more or less identical culturally and immunologically, varying only in virulence.[90] She [51] has shown conclusively, however, that there is a difference between the two groups in the pathogenicity for rabbits. Of seventy respiratory strains only four were pathogenic for rabbits, while eight of nine meningitic strains were pathogenic. Davis [42] failed to find any difference in the virulence of respiratory and meningeal strains. Other observers have usually found the meningeal strains pathogenic for small animals, especially rabbits. Henry [45] isolated from one of his patients with influenzal meningitis a bacillus that was nonpathogenic for laboratory animals. He obtained pathogenic bacilli, however, from some of his other patients. The nonpathogenic

organism was isolated from a patient with a meningitis following a mastoiditis for which an operation was done. At the necropsy the meningitis was localized mostly at the base and on the side of the brain near the site of operation. Perhaps this was an instance of a secondary meningitis produced by an ordinary respiratory strain of *B. influenzae*. In that event the bacillus would be expected to have the pathogenicity as well as the serologic reactions of an ordinary respiratory strain. I have tested the pathogenicity of five meningeal strains and found that all of them, when first isolated, killed rabbits in small intravenous doses. The few respiratory strains so far tested have failed to do so.

DISCUSSION

The facts in this paper are not presented as conclusive evidence that influenzal meningitis in the majority of instances is a primary disease. They are suggestive enough, however, to indicate that such may be the case and to show how the disease should be thought of and studied in the future. The idea that it is a primary disease caused by the special group of *B. influenzae* does not exclude the possibility that it may at times be secondary and produced by ordinary respiratory strains of influenza bacilli, nor does it exclude the possibility that the meningitic strains may occasionally produce diseases other than meningitis.

Treatments of various kinds have been used, but as far as can be determined none has accomplished much. Even the serum [72] produced by Wollstein [91] has not given the results expected.[51] It may be, since more is now known of the biologic and the serologic reactions of meningitic strains of influenza bacilli, that a better treatment serum can be produced.

SUMMARY

The records of 197 cases of influenzal meningitis have been reviewed and twenty-three new cases are reported.

Influenzal meningitis is a disease of infancy, 79 per cent. of cases occurring in patients under 2 years of age.

The mortality in 220 cases was 92 per cent. Of the seventeen patients who recovered twelve were 2 years of age or older.

There is no typical clinical picture of influenzal meningitis. Many cases are probably overlooked.

There is usually a polymorphonuclear leukocytosis.

From the case records it is possible to say that the meningitis might have been primary in the majority of instances.

Influenzal meningitis is probably a carrier-borne disease.

The seasonal and yearly incidence of influenzal meningitis and of epidemic influenza and pneumonia do not coincide.

The meningitic strains of influenza bacilli are closely allied to each other and differ from the ordinary respiratory strains of *B. influenzae*,

particularly in their serologic reactions and in their pathogenicity for rabbits.

CONCLUSIONS

Influenzal meningitis appears to be in most instances a primary disease produced by a group of influenza bacilli which are closely allied culturally and serologically.[92]

BIBLIOGRAPHY

1. Dunn, C. H.: Am. J. Dis. Child. **1**:95 (Jan.) 1911.
2. Neal, J. B.: Arch. Pediat. **38**:1, 1921.
3. Rivers, T. M., and Kohn, L. A.: J. Exper. M. **34**:477, 1921.
4. Fraenkel, E.: Ztschr. f. Hyg. **27**:315, 1898.
5. Slawyk: Ztschr. f. Hyg. **32**:443, 1899.
6. Meunier, H.: Compt. rénd. Soc. de biol. **52**:5, 1900.
7. Trăilescu, I: Spitalul Rev. Med. **21**:474, 1901.
8. Langer, J.: Jahrb. f. Kinderh. **53**:91, 1901.
9. Dubois: Thèse de Paris, Nov. 27, 1902, No. 49. Cited by Adams: Arch. Pediat. **24**:721, 1907.
10. Ghon, A.: Wien. klin. Wchnschr. **15**:667, 1902.
11. Cagnetto, G.: Atti d. Reale Inst. Veneto **63**: Pt. 2, 397, 1903.
12. Costinesco: Congress Internat. d. Med., 1903, Pediat. Sec., p. 967.
13. Mya, G.: Gaz. d. 'Osp. **24**:268, 1903.
14. Mya: Riv. clin. Pediat. **1**:465, 1903.
15. Thomesco and Grascoski: Bull. de la Soc. des Sc. Méd. de Bucharest, 1904, No. 2. Abstracted: Rév. neurol. **13**:44, 1905.
16. Jundell, I.: Jahrb. f. Kinderh. **59**:777, 1904.
17. Bertini, E.: Riv. clin. Pediat. **2**:673, 1904.
18. Cattaneo, C.: Rend. d. Assn. med.-chir. di Parma **6**:115, 1905. Abstr. Centralbl. f. Bakteriol. (Ref.) **39**:455, 1907.
19. Simon, G. L.: Rev. mens. d. mal. de l'enf. **23**:271, 1905.
20. Dudgeon, L. S., and Adams, J. E.: Lancet **2**:684, 1907.
21. Sprigg, W. M.: Am. J. Obst. **56**:467, 1907.
22. Douglas, J. Sh. C.: Lancet **1**:86, 1907.
23. Saathoff: München. med. Wchnschr. **54**:2220, 1907.
24. Adams, S. S.: Arch. Pediat. **24**:721, 1907.
25. Bentz, C. A., and Frye, M. J.: Woman's M. J. **18**:73, 1908.
26. McDonald, S.: J. Path. & Bacteriol. **12**:442, 1908.
27. Hymanson, A.: New York M. J. **90**:1268, 1909.
28. Cohen: Ann. de l'Inst. Pasteur **23**:273, 1909.
29. Cohoe, B. A.: Am. J. M. Sc. **137**:74, 1909.
30. Davis, D. J.: Arch. Int. Med. **4**:323 (Sept.) 1909.
31. Simon and Aime: Semaine méd. **30**:513, 1910.
32. Simon, G.: Monatschr. f. Kinderh. **9**:549, 1910.
33. Batten, F. E.: Lancet **1**:1677, 1910.
34. Ager, L. C., and Avery, O. T.: Arch. Pediat. **27**:284, 1910.
35. Ritchie, J.: J. Path. & Bacteriol. **14**:615, 1910.
36. Sayce, O. A.: Australian M. J. **16**:25, 1911.
37. Clemens, J. R., and Gould, C. W.: Arch. Pediat. **28**:210, 1911.
38. Rhea, L. J.: Arch. Int. Med. **8**:133 (July) 1911.
39. Prasek, E., and Zatelli, T.: Wien. klin. Wchnschr. **24**:932, 1911.
40. Wollstein, M.: Am. J. Dis. Child. **1**:42 (Jan.) 1911.
41. Brem, W. V., and Zeiler, A. H.: Am. J. Dis. Child. **1**:417 (June) 1911.
42. Davis, D. J.: Am. J. Dis. Child. **1**:249 (March) 1911.
43. Jundell, I.: Hygiea Medicinsk och Farmaceutisk Månadsskrift **74**:326, 1912.
44. Klinger, R.: Cor.-Bl. f. schweiz. Aerzte **42**:1289, 1912.
45. Henry, H.: J. Path. & Bacteriol. **17**:174, 1912.
46. Giese, H.: Ugesk. f. Læger **75**:621, 1913.

47. Ducrot: Rev. Méd. de la Franche-comité **21**:195, 1913.
48. Grasty, T. S. D.: Am. J. Obst. **67**:1031, 1913.
49. Ross, A., and Moore, A. E.: Brit. M. J. **2**:1056, 1913.
50. Spillman, P., and Benech, J.: Province méd. **24**:433, 1913.
51. Wollstein, M.: Tr. Fifteenth Internat. Congr. Hyg. and Demog. **2**:57, 1913.
52. Atkinson, E.: M. J. Australia **1**:421, 1914.
53. Tebbutt, A. H.: M. J. Australia **1**:415, 1914.
54. Nyberg, C.: Finska Läk.-Sällsk. Handl. **57**:1369, 1915.
55. Ely, F. A., and Weingart, J.: J. Iowa State M. S. **5**:391, 1915.
56. Imperatori, C. J.: Laryngoscope **25**:580, 1915.
57. Cleland, J. B., and Ferguson, E. W.: M. J. Australia **1**:308, 1915.
58. Brown, A.: Canad. M. A. J. **5**:1077, 1915.
59. Boland, C. V.: Lancet **2**:704, 1915.
60. Hill, R. B., and Packard, R. J.: Lancet-Clinic **113**:723, 1915.
61. Aaser, E.: Tidsskr. f. d. norske Lægefor. **36**:393, 1916.
62. Packard, F. R.: Ann. Otol., Rhinol. & Laryngol. **25**:706, 1916.
63. Moody, E. E.: J. Missouri State M. A. **13**:328, 1916.
64. Williams, E. H.: New Zealand M. J. **15**:48, 1916.
65. Torrey, R. G.: Am. J. M. Sc. **152**:403, 1916.
66. Bhat, K. S.: Lancet **2**:384, 1917.
67. Tobler, W.: Cor.-Bl. f. schweiz. Aerzte **47**:881, 1917.
68. Lacy, G. R.: J. Lab. & Clin. M. **4**:2, 55, 1918.
69. Hills, R.: New York M. J. **107**:345, 1918.
70. Albert, H., and Kelman, S.: J. Infect. Dis. **25**:433, 1919.
71. Johnson, C. K.: Arch. Pediat. **26**:82, 1919.
72. Dunn, C. H.: Pediatrics **3**:547, 1920.
73. Stone, C. T.: Texas State J. M. **15**:318, 1920.
74. Litchfield, W. F.: M. J. Australia **1**:104, 1920.
75. Christiansen, M., and Kristensen, M.: Ugesk. f. Læger **83**:551, 1921.
76. Finkelstein, H.: Lehrbuch der Säuglingskrankh., Ed. 2, Berlin, 1921, p. 571.
77. Abt, I. A., and Tumpeer, I. H.: Am. J. Dis. Child. **21**:444 (Nov.) 1921.
78. Rivers, T. M.: Bull. Johns Hopkins Hosp. **30**:129, 1919.
79. Rivers, T. M.: J. A. M. A. **75**:1495 (Nov. 27) 1920.
80. Flexner, S.: J. A. M. A. **67**:16 (July 3) 1911.
81. Jordan, E. O.: J. A. M. A. **74**:623 (Feb. 28) 1920.
82. Personal Communication.
83. Jordan, E. O.: Interepidemic Influenza, De Lamar Lecture, School of Hygiene, Johns Hopkins University, Jan. 31, 1922.
84. Holt, L. E.: Am. J. Dis. Child. **1**:26 (Jan.) 1911.
85. Povitsky, O. R., and Denny, H. T.: J. Immunol. **6**:65, 1921.
86. Valentine, E., and Cooper, G. M.: J. Immunol. **4**:359, 1919.
87. Chesney, A. M.: J. Infect. Dis. **29**:132, 1921.
88. Anderson, R. A., and Schultz, O. T.: J. Exper. M. **33**:653, 1921.
89. Cohen, Ch., and Fitzgerald, J. G.: Centralbl. f. Bakteriol. **56**:464, 1910.
90. Wollstein, M.: J. Exper. M. **22**:445, 1915.
91. Wollstein, M.: J. Exper. M. **14**:73, 1911.

92. After the completion of this paper Dr. I. H. Erb furnished information concerning nine cases of influenzal meningitis observed in the Hospital for Sick Children in Toronto in the last two and one-half years. Of the nine patients seven were under 2 years of age. One case occurred in September and three cases in November, 1919; one in November and one in December, 1920; two in November and one in December, 1921. The mortality was 100 per cent. A necropsy was obtained in every instance and the meningitis was considered to have been primary in four of the nine patients, 44 per cent.

STUDIES OF NEPHRITIS IN CHILDREN

I. NEPHROSIS *

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During the past three years we have had the opportunity of studying about sixty cases of kidney disease in children. According to the clinical findings these cases seem to have fallen into four groups. By means of laboratory data we have endeavored to strengthen this classification so as to make it useful from a diagnostic and therapeutic standpoint:

Group I comprises cases which began either without apparent cause, in children seemingly in perfect health, or in which the mother had, perhaps, noticed that the child was pale. There was little or no elevation of temperature and apparently no accompanying disease. Edema of the face or legs first appeared. It spread rapidly to the remainder of the body. The edema was very persistent, or if it did disappear it showed a decided tendency to recur. There was no hematuria but the urine, at times, was diminished in quantity and always contained large quantities of albumin. The edema was the outstanding feature. The duration of the disease was months or years, and the patient showed no tendency to get well. This malady is known in the earlier literature as nephritis parenchymatosa and has more recently been termed nephrosis by Volhard.[1] Others have used the terms nephropathia epithalialis, nephropathia tubularis and epithelial nephrosis.

Group II comprises cases which began acutely with or without an accompanying acute disease, often with temperature elevation and with or without edema, the edema usually being not extensive, often localized to the face, or to the face and the extremities, and never very persistent. Hematuria was a common symptom. The cases usually lasted a few weeks; occasionally they became subacute and the symptoms would continue a few months, or become chronic and extend for years. Cases of this type are known in the literature as acute nephritis, acute hemorrhagic nephritis or acute glomerulonephritis. When chronic, they are termed chronic glomerulonephritis.

Group III comprises cases observed in private practice for a period of months or years accompanied by an occasional acute stage, but with

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* From the Pediatric Service and Pathologic Laboratory, Department of Physiologic Chemistry, Mount Sinai Hospital.

1. Volhard, F.: Die Doppelseitige Haematogischen Nierenkrankheiten, Berlin, 1918.

none of the outward signs usually seen in kidney disease, such as edema, hematuria or high blood pressure. They are the cases termed by Heubner [2] "paedonephritis."

Group IV comprises cases characterized by marked pallor, headache, vomiting, polyuria, high blood pressure, retinitis, convulsions and death. The entire duration of the disease was about one year. Cases of this description are similar to the contracted kidney, or nephritis with hypertension of the adult.

GROUP I: THE NEPHROSES

The first group to be discussed is the nephroses. These are so named by Volhard [1] and in most of our textbooks they are termed "nephritis parenchymatosa." We use this term strictly in a clinical sense, not having had the opportunity to verify or to classify these cases

TABLE 1.—POSSIBLE REMOTE ETIOLOGIC FACTORS

Previous History	No. Cases	Years Ago
Scarlet fever	1	7
Measles	2	6
Measles	1	5
Measles	1	4
Measles	1	3
Measles	1	1
Pertussis	1	6
Pneumonia	2	5
Cervical adenitis	1	3
No infectious diseases	4	

TABLE 2.—RECENT POSSIBLE ETIOLOGIC FACTOR

Case	Disease	No. Cases	When
5	Tonsillitis	1	Six weeks before onset of disease
7	Tuberculosis	1	Many months before and during disease
8	Scarlet fever	1	Four months before onset of disease
11	Diphtheria	1	Four months before onset of disease
14	Otitis	1	Concomitant with onset of disease
16	Scarlet fever (?)	1	Four weeks before onset of disease

from a pathologic standpoint. There are seventeen cases in which histories and general course conform more or less to the description given above.

ETIOLOGY.—In discussing this type of kidney disease and, in fact, in all disease, it is important to examine closely the life history of the patient; for example, a systolic murmur at the apex demands more consideration if one knows there has been a previous chorea.

In Table 1 it will be seen that as a remote etiologic factor only one patient had scarlet fever; five patients had measles, one pertussis, one pneumonia, one adenitis and four had no infectious diseases whatever.

2. Heubner, O.: Kinderkrank., Ed. 3 **2**: p. 502.

Although most of these cases did not exhibit an acute condition at the onset of the symptoms, in Table 2 we have tabulated some of the recent acute diseases of these patients. In eleven cases there had been no recent disease so far as we could ascertain, but in five cases some recent disease had preceded this onset.

In analyzing the history of some of these cases, it is interesting to note that one patient (Case 5) had scarlet fever seven years ago. Whether the kidney was damaged at that time and whether the recent tonsillitis was an exciting factor, cannot be determined, for unfortunately we have no accurate interviewing history. Another patient (Case 14) had a recent otitis, otherwise was apparently well but had always had a sallow complexion. A third patient (Case 8) had a questionable scarlet fever four months previously, but was apparently well until swelling of the face was first noted. As is well known, the toxin of scarlet fever usually affects the vascular and not the tubular portion of the kidney which is said to be the lesion in nephrosis. Yet at times, as Heubner [3] has shown pathologically, a tubular nephritis may develop during the course of a scarlet fever infection. Case 16 is a similar one which seemed to develop soon after an attack of a possible scarlet fever, for a sister in the family had scarlet fever at that time. It may, therefore, be possible that the virus of scarlet fever may, at times, give this clinical picture.

As is proven by Volhard's [1] statistics, tuberculosis may be the etiologic factor, for of fifty-five cases of nephrosis cited, fifteen had tuberculosis. Only one of our cases had a possible tubercular etiology. The Pirquet reactions in the remaining cases were negative.

Case 2 is of interest, the patient having had diphtheria a short time previously. In diphtheria, in contrast to scarlet fever, there may be a distinct tubular involvement of the kidney. The diphtheria toxin given intravenously to animals regularly produces an involvement of the kidney tubules, and at the height of the disease albumin and casts appear. Feldman [4] found an involvement of the kidney in 12 per cent. of his cases of diphtheria. Dorner [5] found this type of kidney disease in 6.7 per cent. of his cases. Edema, however, was rarely present, and hematuria and a rise in blood pressure were absent. An interesting clinical fact worth noting is that of Feldman's seventy-three cases of diphtheria complicated by a nephrosis, forty-three patients died, showing the added gravity of this condition in diphtheria. Very few of the cases which recover from diphtheria, however, result in this form of kidney disease.

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3. Heubner, O.: Jahrb. f. Kinderh. **77**:1, 1913.
4. Feldman, H.: Monatschr. f. Kinderh. **19**:491, 1921.
5. Dorner, G.: Quoted by Feldman, Klin. Stud. z. Path. in Behand. der Diphth. Jena, 1918.

Syphilis may cause a symptom complex similar to the one we have studied. Munk [6] describes the clinical picture as one with marked anemia, edema, oliguria, albuminuria, casts and low blood pressure. In our cases the Wassermann reaction was uniformly negative.

Exposure.—Inasmuch as exposure to cold has often been described as an etiologic and exciting cause of kidney disease, it was interesting to see at what time of the year the symptoms in our cases were first noted. It was found that eight cases began in the cold months and nine in the warm months. Although so few cases have been studied, cold or exposure cannot be an important causative factor.

Sex.—Sex seems not to be a predisposing cause. Eight of the patients were females and nine were males.

Age.—Ten of the seventeen patients were of the preschool age giving, perhaps, added evidence of the unimportance of the infectious diseases (Table 3).

There remains, therefore, a considerable number of these cases without any known etiologic factor: the genuine "nephrosis" cases of

TABLE 3.—AGE OF PATIENTS

Age, Years	No. Cases
2	1
3-4	5
5	4
6-7	3
8-9	1
10-11	2

Volhard. He, as well as Epstein,[7] repeatedly pointed to a general metabolic disturbance, perhaps of the ductless glands, as a cause of this disease, and that these cases do not seem to be primarily a disease of the kidney.

SYMPTOMS: *Onset.*—In some of our cases there was a history of pallor or a generally subnormal condition existing for some months previously. In a few cases there was a distinct history of malaise, vomiting and headache; in the majority of cases, however, the first symptom noticed by the parents, was the swelling about the face, the edema increasing with great rapidity. In ten cases the edema began in the face and within twenty-four hours the legs were involved. In other cases the edema of the legs and face occurred simultaneously, and in the course of about a week the other subcutaneous tissues were also involved.

Temperature.—Temperature elevation was not usually present, and the children were not acutely ill; the throat was generally in fairly

6. Funk, F.: Ztschr. f. klin. Med. **78**:1, 1913.
7. Epstein, A. A.: Am. J. M. Sc. **163**:167, 1922.

good condition, only three of the seventeen patients had enlarged tonsils. These children as contrasted with our cases of acute glomerulonephritis were not of the exudative or lymphatic type.

Heart.—The heart is usually involved whenever there is general anarsaca, and ordinary physical examination often does not show the true picture. Alwens and Moog,[8] by means of careful roentgen-ray measurements and the rapidly changing heart borders, showed that there is a dilatation of the heart in acute nephritis. Wessler,[9] in like manner, showed that there was distinct hypertrophy in cases of chronic nephritis. So, in our cases, by means of the roentgen ray, it was possible to follow the change in the heart outline according to the presence or absence of general edema. From the pictures it can definitely be stated that there is usually a hydropericardium whenever there is marked general edema.

Chest.—In the pleural cavities, fluid is often present, as demonstrated by the roentgen ray when no signs by ordinary physical examination can be elicited. It is impossible to explain just why the left side of the chest seems more often affected. These cases are often complicated by the infection of the bronchi and the lungs.

Abdomen.—The abdominal cavity, like the pericardium and the pleura, is usually involved but to a much greater extent. Ascites was present at one time or another in all our cases and required paracentesis. The character and analysis of these fluids will be detailed in another portion of the paper.

Edema.—Edema of the subcutaneous tissues was present to a greater or lesser degree at all times. Even when there is no demonstrable edema, there is a marked disposition to it. During marked edema the skin and subcutaneous tissues are greatly distended, and there is a tendency to skin infection, which, however, from our experience, seems not as marked as in the adult, for only once did we see an erysipelas.

Edema of the face and brain: Edema of the face is usually present at one time or another. We believe that edema of the brain may also be present and cause cerebral symptoms erroneously termed uremia. Case 15 had such a symptom complex. The child complained of headache, became semiconscious, cyanotic and would cry out, the attack lasting about twenty minutes and recurring a few times in twenty-four hours. A week later the child was in a semicomatose condition for eighteen hours. During these attacks there was no nitrogen retention of the blood, no increased blood pressure and the eyegrounds were normal.

Abdominal Pain.—This is present at times with a great degree of severity and may be located about the umbilicus. This may be due to an edema of the intestinal wall, but a pneumococcus peritonitis must always suggest itself.

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8. Alwens and Moog: Deutsch. Arch. f. klin. Med. **133**:364, 1920.
9. Wessler, H.: Arch. Int. Med. **14**:517 (Nov.) 1914.

Diarrhea.—May occur and is often very severe, this probably being a means of getting rid of the edema fluid. In one of our cases there was a marked diarrhea with mucus and blood, lasting for over two weeks, during which time the ascites and subcutaneous edema disappeared, the child losing 14 pounds in weight.

Anemia.—The anemia in this disease is usually of a mild secondary type, and it is only toward the end of the disease that the hemoglobin may drop below 50 per cent., the red blood cells (Table 4) rarely falling

TABLE 4.—Blood Count

Case No.	Red Blood Cells	Hemoglobin, per Cent.	White Blood Cells	Polymorphonuclears, per Cent.
1	4,840,000	90	7,200	68
2	....	98	17,000	65
3	5.170.000	80	.....	..
	2,150,000	35	22,000	86
4	.....	..	.....	..
5	4,200,000	78	10,000	60
6	3,900,000	80	7,000	70
7	.....	75	9,600	42
8	3,000.000	57	16,000	75
9	4,900,000	85	.....	..
10	4.200,000	80	21,000	80
11	4,100,000	80	12,000	55
12	4,400,000	80	10.000	68
13	.....	..	.....	..
14	3,000.000	65	12.000	50

TABLE 5.—Blood Pressure

Case No.	Age. Years	Blood Pressure		Remarks
		Systolic	Diastolic	
3	6	85	60	
		120	90	Near death
4	..	...	..	
5	11	105	75	
6	5	85	58	
7	10	...	..	
8	4	90	40	
9	8	90	65	
		122	80	
		110	90	No N ret
		AUTHOR: WHAT IS MEANT BY "N ret" ?		
10	5	100	60	
11	3½	105	85	
13	..	...	..	
14	4	95	65	
15	7	120	90	
		125	90	
		135	90	
		130	90	N ret at times
16	2	90	..	
17	7	114	90	

below 3,000,000, there being not much difference in the count before, during or after the disappearance of the anasarca. These children often look very anemic but the absolute degree of anemia is never very great.

Blood Pressure.—The blood pressure (Table 5) is practically normal. In five cases the systolic pressure rose above 115 and reached 135 in one case. The question of blood pressure in children is always a mooted one, a neurotic temperament, crying and other circumstances may make the blood pressure vary. When the children are doing badly

or are near death, as in Case 3, the blood pressure is apt to rise. In Case 15 there was persistently high blood pressure, but only on one occasion was there a high nonprotein nitrogen, later in the disease the nitrogen decreased, yet the systolic blood pressure remained from 125 to 135. Dorner [10] showed that the ingestion of fluid does not cause the blood pressure to rise in cases of nephrosis, for presumably the blood vessels permit water to penetrate into the tissues and no plethora is established. This was confirmed by showing that the total solids of the blood were unchanged. Even intravenous administration of fluid does not cause an increase of the blood pressure. He shows that in addition to increased blood volume there must be a certain contractibility of the blood vessel walls before there can be an increase in blood pressure. In the so-called water test, which will be discussed in detail later, it was observed that the ingestion of large quantities of fluid in a comparatively short time did not increase the blood pressure.

The phenolsulphonephthalein test in these cases showed relatively poor excretion. The test, however, was very unsatisfactory. The dye injected into the edematous tissues is absorbed irregularly and reaches the kidney much more slowly than the two hours alloted to the test, and when given intravenously, the test may also not be accurate because of the permeability of the vessel walls. In one case in which it was given subcutaneously, 25 per cent. of the dye was excreted in two hours with a urine output of 70 c.c.; given intravenously, 32 per cent. was excreted in 100 c.c. of urine. Hessel [11] showed that intravenous injection was, perhaps, a little more satisfactory.

Blood.—The physical character of the blood exhibits a striking quality quite different from the normal, for on drawing blood from the vein and permitting it to coagulate, the serum separates quickly and is distinctly milky, instead of being the normal straw colored, clear serum.

The chemical examination of the blood in the light of the many new microchemical methods which have been devised in the last few years is extremely interesting, examinations being made of the urea, nonprotein nitrogen, uric acid, creatinin, cholesterol, carbon dioxid, sugar, total serum fat and total serum protein and serum chlorids.[12]

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10. Dorner, G.: Deutsch. Arch. f. klin. Med. **133**:21, 1920.
11. Hessel, K.: Deutsch. Arch. f. klin. Med. **114**:396, 1914.
12. *Methods:* Urea—urease (Marshall); nonprotein nitrogen—digestion and titration; uric acid and creatinin with Kuttner's modification of Folin's method; sugar—with Epstein's modification of Benedict's method; cholesterol—Bloor's method; carbon dioxid—Van Slyke's gasometric method; serum chlorids—Van Slyke and Donleary and some by the method of A. S. Wetmore (J. Biol. Chem. **45**:113 [Dec.] 1920); total serum fat—extraction with ether and petrolic ether, using the Roese-Gottlieb method (Rohrig tube); total serum protein—total nitrogen minus nonprotein nitrogen $\times$ 6.25.

From Table 6 it will be seen that the urea nitrogen, the nonprotein nitrogen, uric acid and creatinin nitrogen showed very little or no change from the normal, the addition of protein to the food not seeming to affect these values. In changing from a carbohydrate or a karrel diet to a high protein diet very little increase in these values occur. This blood composition, as we will show in a later portion of the article, is one in marked contrast to that seen in cases of acute and chronic nephritis. The nephroses rarely show any retention of nitrogenous substances in the blood, and thus apparently do not terminate in fatal uremia. The coma and convulsions sometimes seen may be due to an acidosis (Case 8) or to an edema of the brain (Case 15).

Case 3 was an exception. In 1915, the child was in Bellevue Hospital, suffering from edema. He was admitted to Mt. Sinai Hospital

TABLE 6.—NITROGENOUS ELEMENTS IN THE BLOOD

Case	Urea N	N P N	Uric Acid N	Creatinin N	Case	Urea N	N P N	Uric Acid N	Creatinin N
1	21.4	54.6	1.5	1.5	10	15.4	46.7	1.7	1.2
	14.0	60.0	1.4	1.1		14.1	45.5	4.2	1.3
	12.6	39.5			11	16.0	46.9	2.0	1.2
2	12.6	56.0	1.9	1.5		19.6	53.4	1.6	1.7
						16.8	32.2	2.0	1.3
3	114.0	206.0	6.0	9.2	12	18.2	45.5	1.9	1.2
4	19.6					18.2	32.2	1.5	1.0
	14.0				13	12.6	32.9	...	1.2
5	11.2	37.5	2.5	1.3	14	12.2	42.0	1.6	1.2
	11.2	35.0	3.4	1.8		25.2	50.0	5.0	1.5
						21.0	49.0	2.8	1.5
6	22.4	45.0	3.0	1.3		19.6	28.6	1.0	1.0
	14.0	35.5	1.8	1.2	15	23.8	82.0	3.0	1.0
						12.6	49.5	...	...
7	21.0	....	...	1.3		19.6	41.5	1.5	1.4
	22.4	54.5	1.5	1.7		14.4	41.0	2.1	1.0
8	....	87.5	4.0	...		30.0	56.4	1.8	1.3
	14.4	41.7	...	2.6		35.2	51.0	1.5	1.2
	32.0	63.0	4.4	3.1		12.6	37.0	2.4	1.1
	12.6	40.0	4.5	1.5	16	18.2	....	1.5	...
						32.2	66.5	2.0	1.6
9	18.2	35.9	1.3	1.1		47.6	87.6	...	...
	15.4	44.4	3.2	2.1		37.8	75.0	...	...
	18.2	45.6	2.8	1.0					
	21.6	46.7	2.6	1.5	17	11.2	....	...	...

in 1917 with a history of recurring edema. He was readmitted to Mt. Sinai Hospital in 1919. On this last admission the child was in a moribund and comatose condition. The blood analysis was as follows: urea nitrogen, 114; nonprotein nitrogen, 206; uric acid nitrogen, 6; creatinin, 9; cholesterol, 0.424 per cent,, showing an abnormally high nitrogen retention and in addition a great increase in the cholesterol. The fundi were negative. Unfortunately, there were no previous chemical examinations of the blood. But with this marked increase in cholesterol and the history as noted, it is likely that we had a case of nephrosis, the patient dying with the symptoms of uremia.

Serum Protein.—The total serum protein of the blood in this condition as shown by Epstein,[13] Volhard[1] and others is almost always

13. Epstein, A. A.: Am. J. M. Sc. **154**:638, 1917 .

reduced, often markedly so. Normally, the serum protein content of the blood after the second year of life is between 7 and 8 per cent. (Utheim [14]); in our control cases the protein content in most cases was about 7.3 per cent. It is lowest in the prematurely born and gradually increases up to the second year; it is also low in infants with chronic intestinal disturbance of the so-called athreptic type,[15] and in surgical shock.[16] It is high in conditions in which there is a sudden or continuous fluid loss, such as persistent diarrhea and vomiting, without a sufficient fluid intake, as in intestinal intoxication of infants and in asiatic cholera. In analyzing our cases it will be seen from Table 7 that in only one case did the protein content approach the normal. In all other cases it was low, and in seven it was below 5 per cent.

TABLE 7.—Total Serum Protein

Case	Date	Urea N	Total Protein, per Cent.	Sodium Chlorid, Mg.	Remarks
1	12/11/21	12.6	6.2	...	After 2 years illness; no edema
4	11/20/21	19.6	4.2	...	Duration 6 months; edema
	12/12/21	14.2	4.35	...	No edema
5	/21	11.2	5.5	...	Duration 4 months; edema
6	7/22/21	14.0	4.96	6.3	Duration 3 weeks; little edema
	12/ 7/21	11.2	5.4	...	No edema
8	4/ 4/21	14.4	5.6	5.6	7 months illness; edema
	4/30/21	32.5	5.3	...	Edema
	11/19/21	40.0	4.3	...	Very slight edema
9	3/ 9/21	18.2	5.6	...	Duration 9 mos.; not much edema
	4/27/21	18.0	4.46	5.6	Edema
10	4/13/21	15.4	4.81	6.0	Duration 1 year; edema
11	4/25/21	16.8	6.3	4.9	Duration 7 months; no edema
	11/25/21	14.0	4.2	...	Slight edema
12	4/ 1/21	18.2	5.9	6.0	History 5 months; edema
14	10/10/21	19.6	4.13	...	Duration 10 months; moderate edema
15	7/21/21	30.8	5.0	6.7	Duration 7 months; moderate edema
16	4/ 9/21	18.2	5.7	5.5	Duration 1 month; edema
	8/24/21	47.6	7.15	...	Edema
17	12/28/21	11.2	4.2	...	Edema

We cannot, however, definitely assert that the diminished serum protein is proportionate to the intensity or the duration of the disease. One of our severest cases (Case 16; the child finally succumbing) had a serum protein content of 7.15 per cent.; on the other hand, one case (Case 11) had a serum protein content of 6.3 per cent. while in the hospital, and seven months later, although the child was in fairly good condition the protein decreased to 4.2 per cent.

Epstein [7] and others have shown that normally the serum albumin fraction of the total serum protein is 65 per cent., and the globulin

14. Utheim, K.: Am. J. Dis. Child. **20**:366 (Nov.) 1920
15. Marriott, W. McK.: Am. J. Dis. Child. **20**:461 (Dec.) 1920.
16. Smith, H. P.; Belt, A., and Whipple, G. W.: Am. J. Physiol. **52**:72, 1920.

fraction almost 35 per cent. of the total, but that in this type of kidney condition just the reverse is true, the globulin predominates. Unfortunately, we were unable to make these determinations.

The significance of this lowered protein content is difficult to explain, except that it may be one of the factors in the production of the edema. Epstein does not think it is due to the hydremia or migration of serum through the capillary walls. It is true that in some of our cases the plasma volume was altered, the corpuscles in relation to the plasma being reduced in quantity. However, this was not always the case. Nonenbruch,[17] in some experimental work, shows that the change of serum protein does not follow the erythrocyte values. At the end of a saline or gelatin infusion, the protein was lower than could be accounted for by the decrease of the red blood cells. In none of our cases did we find the red cell ration above normal.

Epstein also believes one must take into consideration the tremendous albumin loss in the urine, for these patients pass large amounts of albumin, sometimes for years, even after they are clinically well. We have never seen a case in which the urine was free from albumin, even after three years.

The work of Loeb [18] on the colloidal properties of protein, and that of Palmer, Atchley and R. F. Loeb [19] on the conductivity of salts in the blood when there is a low serum protein may have important bearing on this condition. One must remember, however, that "in vivo" the hydrogen ion concentration and the sodium chlorid content of the blood is constant, the serum protein being the variant in this type of nephritis. These authors suggest a mechanical interference by the protein. Whipple [16] suggests that the protein may exercise a strong stabilizing and protective influence in maintaining a relationship of the circulating blood to the body cells.

Cholesterol and Fat in the Blood.—One of the most striking changes in the chemical composition of the blood in nephrosis is a marked increase in the cholesterol and the fat. This was first pointed out by Chauffard [20] and used by Stepp [21] and Post [22] as an aid in the diagnosis of this form of kidney disease.

Before discussing this phase of the disease, it might be interesting to summarize some of our knowledge concerning cholesterol in the body, and especially in its relation to infants and children. From many examinations of normal children by the methods used in our laboratory

17. Nonenbruch, W.: Arch. f. Exper. Path. u. Pharmakol. **91**:218, 1921.
18. Loeb, J.: J. Gen. Physiol. **1**:237, 363, 483, 559, 1920.
19. Palmer, W. W.; Atchley, D. W., and Loeb, R. F.: J. Gen. Physiol. **3**: 801, 1921.
20. Chauffard, A., and Grigaut, A.: Ann. de méd. **8**:149, 1920.
21. Stepp, W.: Deutsch. Arch. f. klin. Med. **127**:439, 1918.
22. Post, F.: Deutsch. Arch. f. klin. Med. **128**:61, 1918.

and also according to Beumer,[23] Stern,[24] Bloor [25] and others, the cholesterol content of the blood of young infants and children was found to be approximately the same as that of adults, viz. 0.120 per cent. to 0.220 per cent. The cholesterol in breast milk [26] is very low during the first day of lactation (0.00035 per cent.), then increases rapidly, so that at the end of the first week it is 0.052 per cent., and at the end of the fifth week it again has decreased. This increase in the cholesterol may be of great importance in the new-born period of the child's life. The cholesterol is not found as such in milk but is in the form of an ester.[27] Woman's milk contains 0.139 per cent. and cow's milk 1.26 per cent.; probably a little less than that found in the blood.

The cholesterol content of the various organis of the body has been investigated by Beumer [28] and Chauffard.[20] The suprarenal is the principal depot for cholesterol, containing about 56 gm. of cholesterol per thousand gm. of suprarenal tissue. The liver and kidney contain 2.9 gm. per thousand gm. of the respective tissues, the other organs and tissues containing but a very small amount.

The cholesterol content of the blood is low in all forms of anemia, in moribund conditions, in scarlet fever and in Addison's disease. In rickets, the exudative diathesis, and in cases of edema due to "Mehlnährschaden" [29] it is normal. It is increased in syphilitic aortitis and in some cases of hypertension. Splenectomy [30] causes a distinct rise in the cholesterol content of the blood, and finally the cholesterol content of the blood is markedly increased in the form of nephritis which we are studying.

The metabolism of cholesterol is as yet very little understood. There is according to Blackfan and Gamble [31] a large negative balance in infants, and they believe that cholesterol may be synthetized in the body. The relation of cholesterol to the maintenance of growth does not depend, apparently, on the amount of cholesterol in the food. Wacker and Beck [32] showed that the cholesterol metabolism was dependent on the fat metabolism, and they believe that the cholesterol is carried out with the fat in the stools, thus explaining the negative balance. They showed that the fat partitions in the stools could be altered by giving cholesterol. Chauffard [20] and his co-workers have done a great deal of work in

23. Beumer, H.: Deutsch. Arch. f. klin. Med. **68**:105, 1920.
24. Stern, G.: Ztschr. f. Kinderh. **25**:129, 1920.
25. Bloor, W. R.: J. Biol. Chem. **49**:201, 1921.
26. Wacker, L., and Beck, K. F.: Ztschr. f. Kinderh. **27**:288, 1921.
27. Beuner, H.: Monatsch. f. Kinderh. **15**:581, 1919.
28. Beumer, H.: Monatschr. f. Kinderh. **18**:443, 1920.
29. Beumer, H.: Monatschr. f. Kinderh. **15**:588, 1920.
30. Medick, E.: Biochem. Ztschr. **59**:419, 1914.
31. Blackfan, K. D., and Gamble, J. S.: J. A. M. A. **73**:218 (July 19) 1919.
32. Wacker, L., and Beck, K. F.: Ztschr. f. Kinderh. **29**:331, 1921.

trying to clear up this problem. They attempted to show that the cholesterol metabolism depends on (1) food intake; (2) glands of internal secretion; (3) the liver.

1. When cholesterol is taken with the food, the cholesterol in the serum increases slightly but returns to a normal level soon after.

2. Of the glands of internal secretion the suprarenal alone is to be considered and seems to be the main depot of the cholesterol, but whether cholesterol is secreted there or only stored in the suprarenal is not known. In unilateral suprarenalectomy, Troissier and Grigant [33] showed that the cholesterol in the blood was high for a few days. Stimulation of the splanchnic plexus to the suprarenal vessels increases the cholesterol output.

3. As for the liver and bile, it has been shown that the cholesterol is excreted in the bile, and, in fact, some think it is the precursor of the bile salts,[34] yet the amount excreted does not approach the total cholesterol destroyed and, perhaps, the liver destroys the remainder (Chauffard).

The intimate association of fat and cholesterol has been pointed out especially by Verse [35] and Bloor.[25] Verse by giving fat alone to rabbits did not produce a lipemia and the animal did poorly, and when he gave cholesterol without fat there was again no lipemia, but the blood cholesterol increased. When he gave cholesterol and fat he produced a lipemia and the animal gained weight. If either one was stopped, the lipemia disappeared. If fat were fed to animals for a time it would take but a little cholesterol to cause a lipemia; but if cholesterol were given alone for a time, it would take a considerable period for the lipemia to develop on giving fat. The blood figures showed better absorption of cholesterol in the presence of fat. The serous cavities in some animals contained fluid, but this fluid had only a very faint trace of cholesterol, but a considerable amount of fat, showing that the fat was more permeable to the capillaries than the cholesterol.

Bloor [25] showed that the normal fat content of the blood is between 0.5 to 0.8 per cent. Milkiness in serum is due to a high fat content, but at times one can get a high fat content without milkiness, as we have seen in some of our cases. After the ingestion of food, he showed there was first an increase of fat in the blood, then of lecithin and finally of cholesterol. The normal lecithin-cholesterol ratio was about 0.96 per cent. Conversely, as the cholesterol was the last to increase in the normal subject so it was also the last to reach its normal level.

The features of a persistent lipemia are: (1) Increase of lecithin and and cholesterol with increase of fat; (2) the greatest increase over

33. Troissier, J., and Grigaut, A.: Presse méd. **20**:1081, 1912.
34. Wacker, L., and Beck. K. F.: Berl. klin. Wchnschr. **58**:453, 1921.
35. Verse, M.: Beitr. z. Path. Anat. u. z. allg. Path. **63**:789, 1917.

the normal is the fat content; next the cholesterol and finally the lecithin. The origin of the fat in a persistent lipemia is (a) food; (b) the fat deposits in the body.

The origin of the lecithin is from a synthesis of the fat and phosphorus of the body. The origin of the cholesterol is unknown,

TABLE 8.—Cholesterin and Fat in Blood

Case	Date	Cholesterin, per Cent.	Fat	Remarks
1	10/10/21	0.200	...	Two years after first admission, no edema at present
3	7/15/19	0.424	1.27	Died soon after admission; very edematous on admission
4	11/21/21	0.628	...	Markedly edematous
	12/12/21	0.360	...	Edema gone
	1/13/22	0.242	...	Edema gone
5	9/ 1/21	0.474	...	Very little edema
	9/17/21	0.450	1.2	No edema
	9/24/21	0.552	...	After fat free diet
	11/18/21	0.592	...	Very edematous
6	7/ 4/21	0.776	...	Very edematous
	7/22/21	0.860	1.6	Edema markedly diminished
	12/ 3/21	0.472	...	Six months later no edema
7	5/ 6/21	0.452	...	Slight edema
	6/23/21	0.420	...	Two weeks later no edema
	12/22/21	0.254	0.59	No edema
8	3/12/21	0.314	...	Comatose; blood CO_2 17 (morphin)
	4/ 1/21	0.616	...	Three weeks later, general condition good; non-protein nitrogen decreased
	4/26/21	0.496	...	Marked diarrhea
	5/11/21	0.418	...	Two weeks later, diarrhea stopped; edema gone
	11/19/21	0.928	...	Six months later, no edema
9	1/24/21	0.412	...	Edema
	3/ 9/21	0.276	...	Edema gone
	4/23/21	0.520	...	Two weeks later, after being home, marked edema
	5/10/21	0.516	...	Marked edema
10	4/12/21	0.464	1.4	Very edematous
	5/28/21	0.352	...	Edema gone
	11/11/21	0.366	...	Edema gone; still in hospital
11	4/12/21	0.592	...	General edema
	3/28/21	0.696	...	General edema
	4/ 6/21	0.424	...	Edema almost gone
	11/15/21	0.376	...	Slight puffiness of face
12	3/31/21	0.284	0.9	Marked edema
	4/13/21	0.170	...	Eleven days after decapsulation, marked edema
	7/19/21	0.334	...	Very edematous
13	10/27/21	0.554	...	General edema
14	5/25/20	0.460	...	General edema
	7/ 6/20	0.648	...	Marked edema
	8/ 4/20	0.430	...	Edema still present
15	3/ 9/19	0.488	...	Edema slight
	4/25/19	0.836	...	No edema
	6/ 1/19	0.738	...	Marked edema
	7/ 1/19	0.532	...	Edema almost gone
	8/11/19	0.616	...	Marked edema; condition poor
	9/20/19	0.464	...	Marked edema
16	5/ 9/21	0.376	...	General edema
	5/13/21	0.532	...	Marked edema; high protein diet begun
	6/25/21	0.388	...	Fourteen days after decapsulation, still edematous
	8/24/21	0.360	...	Still edematous
17	12/28/21	0.740	1.7	General edema

and the cause of the increase in the cholesterol and why it should accompany an increase of fat and lecithin is as yet unsolved.

From Table 8 it will be seen that in every one of our cases the cholesterol content of the blood was markedly increased, with the exception of Case 1. This estimation was not made when the patient was

originally in the hospital, but only recently when she had been free from edema for some time, so that in this case we cannot make a definite diagnosis of nephrosis from the examination of the blood.

Case 4 is interesting for the child was markedly edematous at the time of the first blood examination. The cholesterol was 0.628 per cent. After losing all his edema, in fact, losing 29 pounds in weight, his cholesterol fell to 0.360 per cent. His serum protein and other nitrogen constituents of the blood were undisturbed. Again, in Case 6, when edema was present, cholesterol was 0.860 per cent., and six months later, without edema, it was 0.472 per cent. It would seem that there is some relationship between the edema and the amount of cholesterol in the blood, yet we have so many determinations to the contrary that this is apparently not the case. Thus, in Case 8, with edema, the cholesterol was 0.616 per cent. The child then had a diarrhea, the edema disappeared and the cholesterol went down to 0.36 per cent. Six months later, however, without marked edema during most of this time, the cholesterol had increased to 0.928 per cent.

Decapsulation of the kidney in two cases seemed to have a temporary effect on the amount of cholesterol in the blood.

In our experience we have found nothing which will directly reduce the amount of cholesterol in the blood for any length of time, be it food, thyroid or surgical procedure.

The total fat content of the blood was naturally high, for the total fat includes the lecithin, cholesterol and fatty acids. The determination of lecithin was impossible at the time because of some technical difficulty. The fat metabolism in the cases in which it was studied was apparently normal, although we did not determine the fat partitions in the stool. Feeding of fat or putting the patient on a fat free diet for a week at a time had no effect upon the cholesterol content of the blood.

Basal Metabolism.—Another interesting fact is the relationship of this hypercholesterolanemia to the suprarenal nad other ductless glands. We realize the interrelationship of these glands and discuss them with great reservation. It has been shown by Epstein and Lande [36] in this Institution that the basal metabolism in these cases is much below the normal (Cases 4 and 5). They took into consideration the artificial increase in body weight in determining the metabolic rate. As these patients improve, the basal metabolism approaches nearer to the normal. Furthermore, the successful therapeutic use of thyroid by Eppinger,[37] Epstein [7] and in some of our cases would point to a probable endocrine relationship. Epstein believes that the metabolism is always low when the cholesterol is high, and high when the cholesterol is reduced in

36. Epstein, A. A., and Lande, H.: (Personal communication).
37. Eppinger, H.: Pathologie u. Therapie des Menschlichen Odem., 1917.

amount. Aub, Forman and Bright [38] show that after suprarenalectomy in the cat the basal metabolism was low, but they gave no cholesterol figures.

THE CAUSE OF EDEMA IN NEPHROSIS

The cause of the edema has been the subject of investigation for many years. Many theories have been advanced to explain it. To the kidney, naturally, was ascribed the edema, for one observed so frequently oliguria with edema, and diuresis with the disappearance of the edema. All observers, however, now agree that the kidney is probably the least offending link in the chain of causes. This chain may tentatively be made up of (*a*) physical, biological or chemical change in the blood itself; (*b*) change in the walls of the capillaries; (*c*) change in the physical or chemical composition of the tissue fluids; (*d*) change in the walls of the venules or lymph channels; (*e*) change in the body cells themselves; (*f*) disturbance of the endocrine gland; (*g*) abnormal nervous control; (*h*) pathologic lesions of the kidney.

A discussion of each of these subjects would take us too far afield, and one may be so linked with the others that it is almost impossible to discuss them separately. Yet some of the newer work might be of interest.

The chemical composition of the blood is so changed that it is very tempting to lay the blame here. As shown before, the serum protein content is consistently diminished, yet this is not the case when edema occurs from some other cause. This decrease in blood protein is not necessarily due to a change in the blood volume and the presence of a hydremia. This was well illustrated in Case 4. The serum protein content was 4.2 per cent. during general anarsaca. Within a week, a marked diuresis having taken place, the child lost 29 pounds in weight and all manifest edema had disappeared, yet the blood protein remained the same. It would not appear, therefore, that the reduction in the protein content of the blood is a great factor.

The sodium chlorid content of the blood did not vary much, never going above 6.1 mg. or below 5.1 mg. per 100 c.c. of blood, independent of the presence or absence of edema. These figures were obtained on a fasting stomach. Atchley [39] showed that there may be no change in the sodium chlorid content of the blood plasma, independent of intake or urinary excretion and, paradoxical as it may seem, to the apparent chlorid balance.

Oehm [40] has recently reported some interesting experiments in relation to the control of diuresis by means of the physical and chemical

38. Aug. J. C.; Forman, J., and Bright, E. M.: Am. J. Physiol. (Proc.) **58**:293, 1921.
39. Atchley, D. W.: Arch. Int. Med. **22**:370 (Sept.) 1918.
40. Oehm, C.: Verhandl. des Congress f. inn. Med., 1920, p. 137.

composition of the blood. He uses two sets of animals—one fed on a dry diet, and the other on a moist diet. During the experiment he repeatedly determined hemoglobin, the serum protein and the sodium chlorid. In both sets of animals the water from the blood goes into the tissue and carries along with it the protein. In the dry fed animals more water remained in the blood than in the moist fed animals, so that the blood was just as rapidly diluted. There is no hydremia in the case of moist fed animals to account for the diuresis which occurs. In tying off the kidneys in both sets of animals there is no difference in the chemical composition of the blood.

The high cholesterol content of the blood does not seem to have any relation to the transudation of fluid and the causation of edema, for, as we will show, there is little or no cholesterol permitted to go through the walls of the capillaries into the edema fluid. It is well known that there is a constant interchange of water, organic and inorganic substances, from the blood into the tissue spaces, thence to the cells and back to the tissue spaces. MacCallum [41] showed that there was no direct connection between the lymph spaces and the tissue spaces and that the lymph channels ended in a blind pouch.

It is important, therefore, to differentiate between (*a*) transudate, (*b*) tissue fluids and (*c*) lymph fluids.

(*a*) Transudate is that fluid which goes through the walls of the capillaries. It may be normal or pathologic.

(*b*) Tissue fluids are that part of a transudate taken up by the cells and given off by the cells.

(*c*) Lymph is that fluid which flows out of the lymph channels. Fluids and other substances from the blood must pass through these tissue spaces before going to all the organs and returning to the blood.

After hemorrhage there is a marked flow of tissue fluid into the blood. This is not from the lymph for there is no demonstrable increase of lymph flow from the lymphatics. Conversely, after transfusion there is a flow of fluid towards the tissues.

Magnus [42] found that 19 per cent. of fluid given intravenously had left the blood stream in three minutes and 50 per cent. had left it in twenty minutes. The injection of hypotonic salt solution causes an exodus of water into the tissues, and salt into the blood. The composition of the blood remains fairly constant. It seems to be the function of the walls of the capillaries to permit the exit or entrance of fluid and other substances into the blood stream, whenever the balance between blood and tissues is disturbed.

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41. MacCallum, W. G.: Text Book of Pathology, 1916, p. 41.
42. Magnus, R.: Arch. f. exper. Path. u. Pharmakol. **42**:250, 1899; **44**:68, 1900.

Hooker,[43] and more recently, Wallace and Pellini,[44] have demonstrated specific capillary poisons which permit of great permeability and this way be the cause of graver general disturbances in the body. Some of these poisons have a selective action on capillaries of certain parts of the body as those of the liver. It is tempting to consider the cause of the disease we are describing as due to a capillary poison acting especially on the skin, muscle and perhaps kidney capillaries.

From the physicochemical standpoint Priestley[45] thinks that the interchange of fluids may be due to a diminution in the electrical conductivity of the plasma, and a difference in what he calls the diffuse pressure. He has likened the blood to a gas, and has tried to explain the diffusion of fluids out of and into the blood stream by the same laws as govern gases. He defines the diffusion pressure of water on both sides of the membrane, as proportioned to the water molecules and the total molecules.

An analysis of the tissue fluids themselves might help to clear up the problem (Table 9). Unfortunately, it is impossible to obtain fluid from the interstices of the tissues in the normal person. In various forms of edema, however, it is shown that these tissue fluids differ. Beckman,[46] who has examined a great variety of edema fluids, has shown that the edema fluids in the nephrosis cases contain only 0.1 per cent. protein. In our cases it was never higher than 0.18 per cent. In the cardiac, the protein content was 0.4 per cent. and in the nephritic the protein content was often over 1 per cent. It will be seen, therefore, that in edema from various causes the vessel walls will differ as to their permeability to protein. Whether 0.1 per cent. protein, as occurs in nephrosis, is greater than the normal cannot be stated. It is this permeability of the vessel wall to protein that Eppinger[37] called the albuminuria of the tissues and is a feature of all edema fluids.

The sodium chlorid content of the various edema fluids is about the same, 0.6 per cent. Thannhauser[47] gave sodium chlorid to nephritics and found that the sodium chlorid of the edema fluid and the blood increased, but the latter, however, to a lesser extent. Soon, however, the sodium chlorid of the blood and edema fluid diminished rapidly, but there was no increase of the salt in the urine. Beckman[46] believes that there is another depot for the salts which is probably the tissue cells.

The cholesterol content of the edema fluids is practically nil. Apparently, the capillary wall is impermeable to this substance.

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43. Hooker, D. R.: Physiol. Rev. **1**:112, 1921.
44. Wallace, G. B., and Pellini, E. J.: Arch. Int. Med. **28**:711 (Dec.) 1921
45. Priestly, G. J.: J. Physiol. **55**:306, 1921.
46. Beckman, K.: Deutsch. Arch. f. klin. Med. **135**:39, 1921.
47. Thannhauser, S. J.: Ztschr. f. klin. Med. **89**:181, 1920.

The relation of the endocrine glands to edema has been emphasized by Eppinger in his monograph. Thevenat [48] was the first to use thyroid as a diuretic. Soon afterward Eppinger began his studies of thyroid extract as an effective diuretic in edema and especially in the so-called nephrotic edema. The manner in which it works is not definitely known. He concluded that it had no specific action on the kidney. He has proven that water and salt are excreted more rapidly after the administration of thyroid. Under normal conditions salt given subcutaneously is excreted more rapidly than if given by mouth. In some abnormal conditions, especially in nephrosis, salt given subcutaneously is excreted less rapidly than that given by mouth. If thyroid is administered the patient will have an excretion which is normal or above normal. Hence,

TABLE 9.—ANALYSIS OF EDEMA FLUIDS

Case No.	Diagnosis	Specific Gravity	Protein	Sodium Chlorid	Cholesterin	Fat
13	Nephrosis	1.0059	.....	0.64	0.212	....
5	Nephrosis	1.010	0.187	0.65	None	0.03
4	Nephrosis	1.010	.....	....	None	....
16	Nephrosis	.....	.....	....	Trace	....
	Cardiac	1.010	0.412	0.66	.....	....

Analysis of Edema Fluids (Beckman [46])

Diagnosis	Protein	Sugar
Nephrosis	0.1	0.123
Nephritics	1.0	0.116
Cardiac	0.4	0.127
Cachexia	0.2	.....

Ascitic Fluids

14	Urea N per 100 c.c.				19.6	36
	N. P. N. per 100 c.c.				28.6	70
	Uric acid per 100 c.c.				1.5	
	Creatinin per 100 c.c.				1.0	
	(Cardiac)	Total N..... 0.256	Protein..... 1.69		Sp. Gr. 1.015	
		Cholesterin... 0.020				
		NaCl..... 0.62				
		Bile plus				

Eppinger believes that there is certainly no selective action on the kidney. Epstein [36] believes that the thyroid increases the basal metabolism. The specific dynamic action of the protein is raised and the colloidal combination of protein in the tissue fluids is changed, thus perhaps setting free the water in the tissues. The hypophysis, on the other hand, has a direct action on the kidney (Oehm [40]).

Oehm has shown that there is a substance in the duodenal mucosa that has a diuretic action. He also thinks that products of metabolism simultaneously stimulate the tissues and the kidney.

That the central nervous system may have some control of the water excretion is shown in some of the intracranial diseases, notably in the disturbance of the hypophysis or tumors of the posterior fossa. The

48. Thevenat, L.: Progrès. méd., 1913, p. 237.

experimental work of Veil [49] and Leschkes,[50] demonstrated that injury to the brain in the region of the fourth ventricle causes a polyuria with a hyperchlorinemia, whereas an injury to the midbrain produced polyuria but no hyperchlorinemia.

It has been known for a long time that section of the renal nerve to one kidney causes an increased flow of urine on that side. This is probably due to a circulatory disturbance in the kidney. E. K. Marshall and A. C. Koll [51] have confirmed this observation, but have also shown that identical results can be obtained by section of one splantic nerve to the suprarenal or removing one of the suprarenal glands.

From the foregoing it will be seen how complex is the problem of fluid excretion.

WATER TEST

In considering the many important and interesting facts already cited, and realizing the importance of the extra renal element, it must not be forgotten that the excretion of water by the kidney gives some very valuable information after all. Many functional kidney tests have been described, such as the excretion of dye stuffs, or salt, of urea and of water. We cannot go into a discussion as to the value of all these tests.

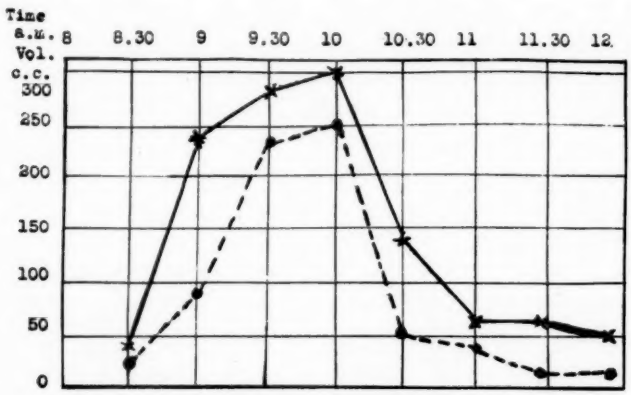
In the course of our work it appeared to us that the excretion of water alone or water with the addition of salt gave considerable information. The test could be carried out very easily and done at home without any difficulty. However, we were very careful with the salt in our nephrosis cases, so that we finally confined ourselves to the administration of water alone. For a long time it has been known that water ingested by a normal person is excreted in a fairly regular manner. This fact was first made use of by Koryani,[52] later amplified by Strauss [53] and finally modified by Volhard.[1] The test for adults is described by Volhard as follows:

> After the usual evening meal the patient is kept in bed for the following one and a half days. At 8 a. m. the patient empties the bladder and this urine is discarded. Immediately after, an adult is given 1½ liters of ordinary water which is swallowed as quickly as possible. No breakfast is given. The patient is asked to urinate every half hour for the next four hours. These specimens are kept separately for further examination. At the end of the four hours, a dry meal is given, such as meat, thick cereal and bread. But no additional fluid of any kind is permitted until the next morning at 8 o'clock. At 6 p. m. another such fluid free meal is permitted. After the first four hours (from 8:30 a. m. to 12:30 p. m.) the patient urinates whenever desired, keeping each specimen separately, the final specimen being collected at 8 a. m., which completes a twenty-four hour cycle. This specimen is preserved. The specimens are examined as to volume and specific gravity.

49. Veil, W. H.: Verhandl. d. Congr. f. inn. Med. **32**:134, 1920.
50. Leschkes, E.: Ztschr. f. klin. Med. **87**:201, 1919.
51. Marshall, E. K., and Koll, A. C.: Am. J. Physiol. **49**:302, 1919.
52. Von Koryani, A.: Physic. Chem. u. Medizin. **2**:133, 1908.
53. Strauss, H.: Chronische Nierenentzündung, Berlin, 1902

It will be seen from the chart that in the normal cases almost the entire fluid ingested will be excreted within the first four hours. The first specimen voided is small in amount, then the volume increases rapidly until the end of the fourth specimen when it begins to drop to a relatively low figure. The specific gravity follows the volumetric change very closely, the urine becoming more and more diluted, the specific gravity often being as low as 1.001 at the end of the third specimen, then it gradually increases so that the specific gravity in the last specimen may be between 1.030 and 1.040.

Of course, in children the amount of water given must be considered. Aschenheim,[54] Stransky and Beiant [55] have investigated the use of this test in infants, and Ohlman [56] in older children. We have



Results of water test; intake, 900 c.c. Amount excreted every thirty minutes for the first four hours. × ——— ×, normal; • — — — •, case of nephrosis.

appended a chart taken from Ohlman [56] which is, however, in the form of percentage intake excreted in twenty-four hours.

The amount of water excreted depends on the age of the child; the younger the child the more water is retained. In a general way it may be said that a normal patient should excrete about the amount ingested at the end of four hours. Of course, this excretion depends somewhat on atmospheric temperature and the activity of the person. The fluid lost by respiration is fairly constant. The addition of salt to the water has a marked effect. The diuresis sets in a little sooner but the total quantity excreted is considerably lower. One other fact must be considered during this test. A person who has been on a dry diet, or a diet comparatively poor in water, will have a much diminished excretion as compared with one who has been on a normal amount of water

54. Aschenheim, E.: Ztschr. f. Kinderh. **24**:281, 1920.
55. Stransky, E., and Balint, A.: Jahrb. f. Kinderh. **93**:350, 1920.
56. Ohlman, J.: Ztschr. f. Kinderh. **26**:296, 1920.

previous to the inauguration of the test. It is important, therefore, to have the amount of fluid to be ingested on the test day about equal to the amount usually taken by the patient.

We must bear in mind from the work of Priestley [45] that the kidney has optimum excretory power per certain unit of time.[57] He gave larger amounts of water to normal persons hour after hour and found that the kidney would not or could not excrete more than a certain amount in a given period of time. Priestley does not believe that there is any great relation between the water and the salt excretion. After drinking 2 liters of water there is a transitory increase in the absolute

TABLE 10.—NORMAL WATER TEST—940 C.C.

Time	Volume, C.c.	Specific Gravity
8:30 a.m.	40	1.010
9:00 a.m.	240	1.004
9:30 a.m.	290	1.008
10:00 a.m.	300	1.008
10:30 a.m.	140	1.008
11:00 a.m.	60	1.010
11:30 a.m.	60	1.012
12:00 m.	50	1.014
Total	1,180	
8:30 p.m.	430	1.030
8:00 a.m.	140	1.040
Full total	1,750	

TABLE 11.—WATER TEST IN NORMAL CHILDREN (FROM OHLMAN) [50]

Age	Water Intake, C.c.	Excretion in 5 Hours, %	Excretion in 5 Hours if 0.7 per Cent. Salt is Added, %
First 6 months	100	60 to 80	27 to 43
Second 6 months	200	80 to 90	49 to 70
1 to 4 years	300	91	70
4 to 6 years	400	133	87
6 to 10 years	600	175	107

amount of chlorid excreted per hour. This washing out, however, lasts only a very short time and a normal chlorid excretion is resumed even though diuresis is increasing.

This water test was used in nine of the reported cases; sometimes only once, other times more frequently. We were careful not to use this test during a period of diminishing edema and only when the condition of the child had been fairly constant for a few days. In judging the amount of water to be given we considered the age of the patient and the amount of urine he was excreting for a few days previously, although always bearing in mind the fact that during the previous days the fluid had not been given all at one time but distributed throughout the day and that food was also given at various times of the day. These facts undoubtedly affect the water excretion.

57. Priestley, J. G., and Haldane, J. S.: J. Physiol. **50**:296, 1916.

RESULTS OF WATER TEST

CASE 1.—A child, aged 11 (Case 5), had very little edema at the time the test was made. Weight, 70 pounds.

The excretion increased rapidly for the first one and one-half hours and then receded rapidly. He did not excrete the entire 1,000 c.c. during the first four hours but did at the end of the twenty-four hours. This retardation we have found to occur frequently in these cases of nephrosis.

A second test, made two and one-half months later, when he was very edematous (weight, 95 pounds), showed much the same characteristics. His diuretic curve was normal. He excreted 500 c.c. of the total in the first four hours, 100 c.c. more than the intake in the twenty-four hours. Only 2 gm. sodium chlorid was excreted during the entire day.

CASE 2.—A child, aged 7 years (Case 4), very edematous, weight being about the same two days before and after the test. On an intake of 500 c.c. he only excreted 250 c.c. Given a water test of 500 c.c. a marked diuretic effect was seen. Why in some instances the ingestion of large quantities of water causes a diuresis at one time and not at others cannot be explained.

TABLE 12.—WATER TEST: CASE 1 (5), 1,000 C.C.

Time	Volume, C.c.	Specific Gravity
8:30 a.m.	50	1.006
9:30 a.m.	150	1.002
10:00 a.m.	200	1.001
10:30 a.m.	200	1.001
11:30 a.m.	25	1.004
12:00 m.	50	1.008
Total	695	
6:00 p.m.	130	1.022
9:00 p.m.	70	1.022
8:00 a.m.	220	1.022

TABLE 13.—WATER TESTS CASE 2 (4), 500 C.C.

Time	Volume, C.c.	Specific Gravity
8:30 a.m.	145	1.024
9:00 a.m.	80	1.004
9:30 a.m.	80	1.003
10:00 a.m.	13	1.005
10:30 a.m.	10	1.010
11:00 a.m.	10	1.012
12:00 m.	10	1.020

CASE 3.—A child, aged 10 years (Case 7), excreted from 300 to 400 c.c. in twenty-four hours for previous few days. It was given 600 c.c. in the water test.

Table 14 shows a normal character to the excretion but a diminished output—357 c.c. of the 600 c.c. excreted in the first four hours; 500 c.c. in twenty-four hours.

CASE 4.—Child aged 4 years (Case 8), with moderate edema. Although the total excretion is good the specific gravity never went above 1.018.

CASE 5.—Child, aged 5½ years (Case 11), with moderate edema. The first water test was followed by a marked diuresis. One month later, the boy, being in about the same condition, was given 500 c.c. but only excreted 250 c.c. in the first four hours and 326 c.c. in the twenty-four hours. We are unable to explain this difference. The concentration in both specimens was normal.

CASE 6.—A child, aged 5 years (Case 14), had been edematous for a long time, the weight changing but little. From Table 16 it will be seen that the excretory curve is a little different from that of other cases. The diuresis continued for a longer period and no single specimen contained more than 100 c.c. Either the water was not brought to the kidney to be excreted, or the kidney did not have the power to eliminate the fluid.

In conclusion, it is quite evident that the manner in which the water is excreted in this type of case in most instances approaches very close to the normal. At times the total quantity excreted is not quite up to the normal. It seems remarkable that an individual with such marked edema should, when given large quantities of water, excrete most of it in a short time; very little is retained, showing well that the excretory power of the kidney is not diminished. Either this water goes directly

TABLE 14.—WATER TEST: CASE 3 (7), 600 C.c.

Time	Volume, C.c.	Specific Gravity
9:00 a.m.	125	1.004
10:00 a.m.	162	1.001
11:00 a.m.	20	1.004
12:00 m.	50	1.007
Total	357	
1:00 p.m.	20	1.010
5:00 p.m.	46	1.024
8:00 p.m.	22	1.028
5:30 a.m.	31	1.024
8:00 a.m.	19	1.024

TABLE 15.—WATER TEST: CASE 4 (8), 800 C.c.

Time	Volume, C.c.	Specific Gravity
8:30 a.m.	57	1.010
9:00 a.m.	145	1.012
9:30 a.m.	153	1.002
10:00 a.m.	165	1.002
10:30 a.m.	130	1.002
11:00 a.m.	45	1.002
11:30 a.m.	27	1.010
12:00 m.	27	1.006
Total	749	
5:00 p.m.	45	1 016
4:00 a.m.	105	1.018
8:00 a.m.	40	1.014

TABLE 16.—WATER TEST: CASE 6 (14), 600 C.c.

Time	Volume, C.c.	Specific Gravity
8:30 a.m.	60	1.002
9:00 a.m.	50	1.002
9:30 a.m.	100	1.002
10:00 a.m.	50	1.002
10:30 a.m.	100	1.002
11:00 a.m.	60	1.004
11:30 a.m.	50	1.006
12:00 m.	20	1.004
Total	490	
8:00 a.m.	20	1.012

into the tissues and other fluid is brought to the kidney, or this water goes directly to the kidney, the tissues being so saturated that they do not take up any more fluid.

Urine.—The ordinary chemical and microscopic examination of the urine in this class of case is so well known that one need not go into detail; the usual high specific gravity and the intense albuminuria with comparatively few casts is the common feature. Red blood cells are

occasionally found. Even with a concomitant acute infection, hematuria is not usually present. Funk was the first to find double refractory bodies in the urine. Gluck found these lipoid bodies to be present after giving cholesterin.

Nitrogen excretion is normal. Using a modified Mosenthal diet, in no case was there ever a real nitrogen retention. Sodium chlorid excretion, however, was affected. The sodium chlorid excretion in the urine was almost nil during the edematous stage. During diuresis as much as 25 gm. sodium chlorid was excreted in twenty-four hours. In this latter case the concentration of the sodium chlorid was 0.6 per cent. in a volume of 4,000 c.c.

Complications.—The complications seen in this disease are all due to the diminished immunity which these patients seemed to have for the acute infection. Those involving the skin, such as erysipelas, seem to

TABLE 17.—DURATION AND PROGNOSIS

Case No.	First Seen	Last Seen	Duration	Condition When Last Seen
1	August, 1919	December, 1921	2 yrs. 3 mos.	Albumin ++; no edema; general condition good
2	February, 1919	May, 1919	5 months	Dead; pneumonia
3	1915	July, 1919	4 years	Dead; uremia (?)
4	September, 1921	Jan. 16, 1921	4 months	Condition good; no edema
5	September, 1921	Jan. 14, 1922	4 months	Dead; pneumococ. peritonitis
6	July, 1921	December, 1921	6 months	Urine, albumin ++; no edema
7	January, 1921	January, 1922	1 year	Urine, albumin ++; no edema
8	July, 1920	December, 1921	1½ years	Urine, albumin ++; slight edema
9	July, 1920	December, 1921	1½ years	Urine, albumin ++; no edema; in hospital
10	April, 1920	December, 1921	1¾ years	Urine, albumin ++; slight edema; in hospital
11	August, 1920	December, 1921	17 months	Urine, albumin +; slight edema; cholesterin 0.376%
12	June, 1920	December, 1921	18 months	Albumin ++; slight edema; in hospital
13	October, 1921	December, 1921	2 months	Very marked edema
14	March, 1920	January, 1921	10 months	Dead; diphtheria
15	January, 1919	July, 1921	½ year	Dead; pneumonia (?)
16	March, 1921	November, 1921	8 months	Dead; nephrosis
17	November, 1921	January, 1922	2 months	Dead; pneumococ. peritonitis

be less frequent than similar cases in the adult. One patient died of a complicating diphtheria. Although discovered early, and large doses of antitoxin being given, the membrane spread with remarkable rapidity.

Pneumococcus infection seems especially virulent in every case. When the patient complains of abdominal pain one would always have in mind a pneumococcus peritonitis. Two of our patients (Cases 5 and 17) died of this complication. Two died of pneumonia. True uremia, in the sense of a stupor associated with an increasing nitrogen retention, is rarely seen. When coma supervenes it is not associated with a nitrogen retention and is usually of short duration. It may best be thought of as a temporary cerebral edema.

Prognosis.—From our experience the prognosis of these cases as to life is bad. Six of the seventeen patients died, and none of the

others can be declared well, although some have been observed for more than three years. Of the fatal cases, the duration of one case was two months and another four years. This latter case had a fairly constant edema. Death usually occurs from some intercurrent infection, although one child seemed to die of uremia. Table 17 gives a good idea of the present status of our cases. We hope to give a more detailed picture of the prognosis at some future date. We are continuing our observations on ten of the cases here reported.

Treatment.—In a condition such as this with its chronicity and marked periods of apparent improvement occurring without any definite cause, one must be very cautious in ascribing great value to any one special procedure. In the present state of our knowledge, prevention can hardly be considered. We feel sure that tonsillectomy and the removal of other foci play but a small rôle in the care of these children, except, perhaps, to put them in the best possible condition. As stated before, these children are not usually of the lymphatic type.

The treatment of the disease must necessarily be directed to (*a*) the albuminuria; (*b*) the pathologic changes in the blood, and (*c*) the edema and the oliguria. From our observations we can say that we have been unsuccessful in permanently affecting the albuminuria or the cholesterinemia. Although at times the albuminuria would be less, at other times, while on the same method of treatment, there would be a marked increase in the albuminuria. The casts in the urine would be present or absent for weeks at a time, without any indication of a real benefit to the patients or foretelling a relapse of the symptoms (edema). The high cholesterin in the blood seemed never permanently affected by whatever method of treatment, and at times when all, or nearly all, manifest edema had disappeared the cholesterin values were highest.

There remains, then, the treatment of the edema and, coincidentally, of the oliguria. This has for years been attacked by means of diet, drugs or both. In addition operative procedures have also been employed. The elimination of fluids from the body is the prime object and the many theories by which this may possibly be accomplished have been treated of in previous portions of this article. Practically, we may consider first the restriction of water in the diet. We have tried this in many cases and systematically have given about the amount eliminated by the kidney for a few days previously, or even reduced the amount to a very small fraction of the kidney excretion but have found that this does not cause an elimination of the body fluids and the edema remains. In fact, we have found that the ingestion of large amounts of water within a short period of time, as in the water test, has a marked diuretic effect and the regular administration of this diuretic water shock has been suggested by Dorner [58] and used in some of our

58. Dorner, G.: Med. Klin. **17**:45, 1921.

cases. At the present writing, it is our opinion that almost the normal amount of water according to age can be given to these cases without any harm. The Karrel treatment has been tried and the amount of milk given was considerably less than the amount of fluid according to the age. In some cases this would cause a dimunition of the edema, while in others it had absolutely no effect. Indeed, in the same case it would be effectual at one time, and ineffectual at another. Epstein [59] seems to think that these are different types of the disease, yet when this occurs in the same case, there must be another explanation. It seemed to us that whenever the small amount of salt present in the milk was really an overdose, the edema was unaffected. In regard to other articles of food in these cases, there have been many conflicting opinions. From our observation we can definitely say that only one constituent of diet seems to do harm, and that is the salt. We have seen considerable carbohydrate given, without much effect upon the edema and no change in the chemical composition of the blood. This is also the case with fat and protein.

The administration of protein, in whatever form, has no deleterious effect on the general condition, the edema or the chemical composition of the blood. This brings us to a discussion of excessive amounts of protein in the diet as recommended by Epstein.[7] There can be no doubt that his high protein diet does good in many cases, and it has seemed to us especially in those cases where the patient has been on a very low protein diet previously. It would appear that this is another example of treating the child as a whole; not letting his general condition deteriorate by a very onesided diet, especially in so important a principle as protein. Epstein's explanation of the edema being due to a dimunition of a blood protein caused by excretion of albumin in the urine does not seem to be proven, for in the first place it has been shown by Nonnenbruch [17] that the serum protein of the blood has little to do with the egress of water from the capillaries into the tissues. In the second place, in some of our cases in which we have given large amounts of protein over periods of months, the edema may or may not have disappeared, yet the serum protein of the blood still remains low. The relationship of globulin to the albumin in the blood serum, to which Epstein has drawn attention, we cannot discuss for we have no experience in observing this. As far as our experience with diet in this disease is concerned, it seems that it is best combated by placing the child on a fairly adequate amount of water, an absolutely salt free but normally balanced diet as far as the remainder of the food principles is concerned. Whether it is necessary to give added amounts of protein to make up for the loss in the urine we cannot definitely say for we are

59. Personal communication.

studying this phase of the disease. That large amounts of protein in the food tend to raise the protein in the blood does not seem to be the case.

As far as the treatment of the edema by means of the ordinary diuretics is concerned it can be fairly definitely stated that they are of no avail, and the saline diuretics may be of decided harm. We have used theocin for its supposed direct action on the kidney and have had no beneficial results. The use of thyroid, however, seems to raise the basal metabolism in these cases and in many instances has a miraculous effect on the edema. We have taken the suggestion of Epstein and Lande,[36] have begun with small doses of thyroid and controlled the increase by basal metabolism observations.

Decapsulation was tried in two of our cases with very little or no effect on the edema, the blood chemistry or the general condition. We are aware that in the literature there are a sufficient number of cases published to warrant this procedure, although in our series the result has been nil.

To sum up, then, our treatment of these patients is to keep them in bed while they have any manifest edema, place them in the best hygienic surroundings, on an absolutely salt free diet, with a normal amount of fat and carbohydrate and an amount of protein somewhat in excess of the normal; a fluid intake almost that of the normal. If this does not suffice, we have added thyroid extract in increasing amounts. As far as the cure of the disease is concerned, the reduction of the albumin in the urine, the cholesterin and fat in the blood, this we have been unable to accomplish.

REPORT OF CASES *

CASE 5 (Hospital No. 213050).—Male, aged 11, admitted Sept. 1, 1921. The child had had recurrent edema of about three months' duration, apparently caused by nasopharyngeal infection, but never any hematuria. However, a history of scarlet fever some years previously might point to the nasopharyngeal infection as a cause for a relighting of an old infection of the kidneys, although there were no symptoms in the interim, as far as the history can elucidate. From the chemical examination of the blood for a period of two months, the low blood pressure, high cholesterin, and the recurrent edema, it would seem that this is a case of nephrosis. Thyroid was given beginning with ¾ grain three times a day, gradually increased to 3 grains three times a day. During this time the edema remained about the same and the basal metabolism had not been accelerated, remaining between —20 and —30 per cent. The child did not respond to treatment, although at one time or other on a salt-free diet, a fat-free diet and, for the past two months, on a high protein diet. Whether this condition was of only a few months standing or whether it dated from the scarlet fever, seven years ago, is impossible to state definitely. The child died of lobar pneumonia.

Family History.—Negative.

Previous History.—Measles (time unknown); scarlet fever seven years ago, but no evidence of kidney disease at that time.

* These cases have been selected as illustrating special points made in the text. All the cases studied will appear in the reprints.

Present History.—Just before the present illness, the child had difficulty in swallowing and was told that he had tonsillitis. A week later (six weeks ago) his mother noticed that he had swelling of arms and legs. After three weeks the swelling disappeared entirely. Was out of bed one week when the edema reappeared. He had no nocturia, hematuria or polyuria. His appetite was good and he had no fever.

Physical Examination.—The child was well developed, fairly well nourished. Face: edematous; some enlargement of cervical lymph glands. Heart: apex beat in fifth space and nipple line; second aortic sound exceeds that of the second pulmonic in intensity; faint systolic murmur at apex. Abdomen: shifting dulness. Extremities: some edema of feet.

Laboratory Examination.—Sept. 1, 1921: Hemoglobin, 78 per cent.; erythrocytes, 2,420,000; leukocytes, 10,000; polymorphonuclears, 68 per cent.

Pirquet and Wassermann Tests: negative.

Urine: acid; specific gravity, 1.020; albumin, trace; many hyaline and granular casts.

Blood Pressure: 105/75.

Blood Chemistry: Urea nitrogen, 11.2; nonprotein nitrogen, 37.5; uric acid, 2.5; creatinin, 1.3; cholesterin, 0.474.

The excretion in four hours is fairly good. The amount of the twenty-four hour period is above that of the intake. The concentration is good.

TABLE 21.—URINARY EXCRETION IN CASE 5

September 5: Water Test, 1,000 c.c.

Time	Volume, C.c.	Specific Gravity
8:30 a. m.	50	1.006
9:30 a. m.	150	1.002
10:00 a. m.	200	1.001
10:30 a. m.	200	1.001
11:30 a. m.	25	1.004
12:00 m.	50	1.008
Total	—695	
6:30 p. m.	130	1.022
9:00 p. m.	70	1.022
8:00 a. m.	220	1.022

September 6: Intake, 625 c.c.; excretion, 460 c.c. Weight, 82 pounds and 9 ounces. Fundi, negative.

September 7: On a salt-free diet; fluid limited to 800 c.c.

September 9: Temperature suddenly went up to 104 F.; came down to normal next day, without any apparent cause.

September 12: Edema is very much diminished and the weight has dropped to 78 pounds. Child has been vomiting all day; continued vomiting for two or three days. All food has been excluded and Delafield's mixture given.

September 15: Intake, 700 c.c.; excretion, 600 c.c. Weight, 77 pounds and 14 ounces.

September 17: Thick cereal, eggs and toast added to diet.

Blood Chemistry: Urea nitrogen, 11.2; nonprotein nitrogen, 35; uric acid, 3.4; creatinin, 1.8; cholesterin, 0.450 per cent.

For one week child was put on a fat-free diet and the cholesterin again estimated; the results showed no diminution, rather an increase in the cholesterin of the blood. Cholesterin, 0.592 per cent.

Basal Metabolism: —20 per cent. below normal. Fat in blood serum, 1.2 per cent.

September 28: Blood pressure, 90/70. Patient is out of bed.

October 1: Intake, 700 c.c.; excretion, 650 c.c. Weight, 77 pounds and 4 ounces.

October 2: Nephritic Test Meal (Mosenthal): Water retention, — + 47 c.c.; nitrogen retention, —0.1 gm.; sodium chlorid retention, —0.69 gm.

October 4: After being out of bed for a few days edema returned.

October 7: Still has edema. Urine about the same since admission. Albumin, three plus; hyaline and granular casts; no erythrocytes or leukocytes.

October 26: Phenolsulphonephthalein test, intramuscular: first hour, 25 c.c. (10 per cent.); second hour, 50 c.c. (15 per cent.); total, 25 per cent.

October 27: Phenolsulphonephthalein test, intramuscular: first hour, 50 c.c. (17 per cent.); second hour, 100 c.c. (15 per cent.); total, 32 per cent.

November 9: On high protein diet.

November 21: Blood pressure, 100/70. Edema and weight about the same.

November 25: Water Test.

November 18: Blood Chemistry: Urea nitrogen, 12; cholesterin, 1.552 per cent.; serum protein, 5.58 per cent.; cells, 30 per cent.; plasma, 70 per cent.

December 7: Basal metabolism, —23 per cent.

December 12: Edema Fluid: Protein, 0.188; specific gravity, 1.010; cholesterin, none; fat, 0.03; sodium chlorid, 0.65.

December 26: Weight, 83 pounds and 13 ounces.

Jan. 10, 1922: For the past four or five days child has been running a temperature with marked abdominal pain. Leukocytes, 23,000; polymorphonuclears, 94 per cent. Signs of pneumonia at the right base with a pneumococcus peritonitis.

January 14: Child died. No necropsy obtained.

Case 8 (Hospital No. 208603).—Male, aged 4, admitted March 12, 1921. During his stay in the hospital had considerable abdominal pain and pain on

TABLE 22.—Urinary Excretion After Water Test in Case 5

Time	Volume, C.c.	Specific Gravity
8:30 a. m.	40	1.030
9:00 a. m.	54	1.006
9:30 a. m.	156	1.002
10:00 a. m.	160	1.001
10:30 a. m.	30	1.008
11:00 a. m.	20	1.010
11:30 a. m.	25	1.012
12:00 m.	16	1.014
3:45 p. m.	92	1.024
6:00 a. m.	320	1.016
8:00 a. m.	190	1.014

urinating. Urine, smoky and containing considerable blood. No explanation for the pain. The roentgenograms were negative. The chemistry of the blood showed an increase of nitrogen retention, increase in cholesterin and a marked diminution in carbon dioxid content; this latter due perhaps to the administration of morphin just before admission. While in the hospital he gradually acquired ascites and general edema; then a very severe colitis with mucus and blood in the stools, lasting several weeks. During this time edema and ascites disappeared. When colitis stopped edema reappeared. Finally discharged, June 14, in good general condition; albumin and casts in the urine; increased cholesterin in the blood, but no retention of nitrogen. When reexamined six months later the child was free from edema; urine contained albumin; blood almost 1 per per cent. cholesterin.

Family History.—Negative.

Previous History.—Measles in infancy; tonsillitis and scarlet fever (?) one year ago. No sore throat since.

Present History.—Eight months ago, about four months after the questionable scarlet fever, child's face became swollen, followed by general anasarca. Abdomen tapped. During this time vomited almost every day. After a few weeks the edema disappeared to reappear subsequently two or three times. Two and one-half months ago severe pain in the right side with a temperature of 106 F. Anuria of one day's duration. Following this the urine was bloody for several weeks, and for weeks still had casts in the urine. Six weeks ago blood reappeared and intermittent hematuria has been present ever since. Two

days ago child again had sudden pain in the right side with high temperature and anuria. A discharge from the right ear has persisted for the past six weeks.

Physical Examination.—The boy was semistuporous, face puffy and breath uremic. Tonsils: hypertrophied. Tight ear discharging. Heart, negative. No edema of the body or extremities. Catheterized specimen, 420 c.c. Phlebotomy, 100 c.c. Blood pressure, 100/70. Urine, smoky; albumin, two plus. Many erythrocytes and hyaline and granular casts.

Laboratory Examination.—March 12: Leukocytes, 16,000; polymorphonuclears, 75 per cent.; hemoglobin, 57 per cent.; erythrocytes, 3,000,000.

Blood Chemistry: Nonprotein nitrogen, 87.5; uric acid, 4; creatinin, 2.4; carbon dioxid, 17.6; cholesterin, 0.314 per cent.

Temperature, 102 F. Wassermann test, negative.

The semistuporous condition may have been due to the uremic poisoning as there is considerable nitrogen retention. On the other hand there is a very low carbon dioxid content which may point to an acidosis. Yet this might be due to a dose of morphin given just before admission. Child was put on 800 c.c. of 10 per cent. glucose water.

March 14: During the past few days patient's general condition is slightly improved but he complains of abdominal pain and pain on voiding. This latter may be due to the catheterization which was necessary.

TABLE 23.—URINE EXCRETION IN CASE 8 AFTER WATER TEST

Time	Volume, C.c.	Specific Gravity
8:30 a. m.	57	1.010
9:00 a. m.	145	1.002
9:30 a. m.	153	1.002
10:00 a. m.	165	1.002
10:30 a. m.	130	1.002
11:00 a. m.	45	1.002
11:30 a. m.	27	1.010
12:00 m.	27	1.006
Total 4 hours	749	
5:00 p. m.	45	1.016
4:00 a. m.	105	1.018
8:00 a. m.	40	1.014
Total 24 hours	1,009	

March 17: Sensorium is clear. Blood carbon dioxid, 29.4. Roentgen-ray examination of the kidney region is negative. The phenolsulphonephthalein excretion is 20 per cent.

March 27: Patient's general condition is excellent. On a diet of cereal, toast, spaghetti, fruit, green peas, baked potato and 450 c.c. of fluid consisting of milk only. Thus has a relatively high carbohydrate diet with moderate amount of protein in the form of vegetable and milk protein.

March 30: A water test of 800 c.c. of fluid showed that the first four hour excretion was almost normal, although the concentration was poor.

April 1: Blood Chemistry: Urea nitrogen, 14; nonprotein nitrogen, 46.7; uric acid, 2.6; creatinin, 1.7; cholesterin, 0.616 per cent.; carbon dioxid, 40.4. Total serum protein, 5.6 per cent.

April 8: Under the carbohydrate diet which he has been receiving the blood in his urine had entirely disappeared and edema had also disappeared.

April 11: The edema and ascites again increasing; put on a high protein diet consisting of egg, chicken, green peas, 600 c.c. of milk, small amount of cereal and toast.

April 13: Edema steadily increasing. Weight, April 4, 37 pounds; April 12, 47 pounds.

April 19: First signs of a diarrhea with mucus, blood and pus in the stools. From April 19 to 24 has had attacks of severe abdominal cramps, frequent

movements and his ascites and general edema are entirely disappearing. Put on 600 c.c. of protein milk alone. Weight dropped to 40 pounds.

April 26: Still many bowel movements.

Blood Chemistry: Urea nitrogen, 32.2; nonprotein nitrogen, 63; uric acid, 4.4; creatinin, 2.1; cholesterin, 0.496 per cent. Total serum protein, 5.3 per cent. The stool picture shows gram positive bacteria.

April 30: Weight, 33 pounds, 6 ounces. Intake, 1,000 c.c.; excretion, 1,000 c.c. Diet: skimmed milk, hard boiled eggs, toast and split pea soup.

May 6: Still some diarrhea but very much better. Weight, 33 pounds. Excretion very good.

May 11: Phenolsulphonephthalein test, 35 per cent.

Blood Chemistry: Urea nitrogen, 12.6; nonprotein nitrogen, 40 per cent.; uric acid, 4.5; creatinin, 1.5; cholesterin, 0.418.

Child is out of bed and edema has disappeared.

May 12: Child has had temperature of 103 F., and a rapid recurrence of the edema. The urine contains a good deal of albumin and hyalin casts but no blood.

May 21: Blood pressure, 90/40. The ascites and edema are increasing. Stools are good.

May 24: General condition is very poor. Child is drowsy. Uremia (?); ascites and edema increasing.

May 30: Again frequent bowel movements but no blood in the stool.

June 4: Diarrhea is better. Fundi, negative. Hemoglobin, 72 per cent.

June 14: Home. General condition very good. No edema. Albumin and casts in the urine.

November 19: Seen for reexamination. Has had occasional edema of the face. On a high protein and low fat diet all this time.

Physical Examination.—Child has slight edema of the face and pretibial edema; otherwise negative.

Blood pressure, 100/70. Hemoglobin, 60 per cent.

Blood Chemistry: Nonprotein nitrogen, 56; cholesterin, 0.928 per cent.; serum protein, 4.3; cells, 29 per cent.; serum plasma, 71 per cent.

Urine: Albumin, three plus; no casts.

From this it will be seen that although the child was practically free from edema the cholesterin content is the highest yet obtained in this case.

CASE 11 (Hospital No. 208275).—Male, aged 3½, admitted Feb. 28, 1921. Observed for nine months with a history of edema of six months' duration before admission. The blood nitrogen has never been increased; the blood cholesterin has always been higher than normal, but lowest on last examination. The total serum protein while in the hospital was 6.2 per cent., but has now dropped to 4.2 per cent. The serum has always been milky. The recurrent edema, the absence of increased blood pressure, the urine and blood findings lead us to classify this as a true nephrosis. This case is especially important since the child had diphtheria just before the onset of symptoms.

Family History.—Negative.

Previous History.—Frequent sore throat and enlarged glands. Diphtheria, ten months before admission; tonsils removed two months after diphtheria. Pneumonia, when 2 years old; measles when 1 year old.

Present History.—Six months ago, that is, four months after diphtheria, child's face became swollen, followed by swelling of abdomen and legs. Since then there has been an increasing pallor and weakness, with hematuria on two or three occasions. No headache, vomiting or convulsions. Meat free and salt poor diet for past six months. About ten weeks ago at another hospital in this city where he remained for four weeks. Taken home with generalized edema and passing about 4 ounces of urine a day.

Physical Examination.—Child chronically ill. General edema. Tonsils have been removed. Heart and lungs: negative. Abdomen: distinct fluid wave. Liver: 3 cm. below costal margin. Extremities: moderate edema.

Laboratory Examination.—Pirquet and Wassermann tests, negative. Hemoglobin, 80 per cent.; erythrocytes, 4,100,000; leukocytes, 12,000; polymorphonuclears, 55 per cent. Blood pressure, 100/80.

Urine: Albumin, three plus; many hyalin and granular casts.

Blood Chemistry: Urea nitrogen, 19.6; nonprotein nitrogen, 53.4; uric acid, 2.6; creatinin, 1.7; cholesterin, 0.592 per cent. Serum, milky.

Diet: Fluids limited to 500 c.c.; milk, cracker and zwieback were given.

March 4 to 10: Salt metabolism estimated. Conclusions of this test are marked water retention, moderate sodium chlorid retention, no nitrogen retention. Intake, 500 c.c. per day; average excretion, 250 c.c.

March 28: Child gradually improving. Put on a diet consisting of cereals, milk, toast and ice cream. Water intake and excretion about the same. Weight, 32 pounds.

TABLE 24.—URINE EXCRETION IN CASE 11 WITH AND WITHOUT WATER TEST

March 27: Water Test: Intake, 800 C.c.

Time	Volume, C.c.	Specific Gravity
8:30 a. m.	110	1.012
9:00 a. m.	125	1.003
9:30 a. m.	214	1.003
10:00 a. m.	230	1.002
10:30 a. m.	141	1.001
11:00 a. m.	48	1.008
11:30 a. m.	14	1.012
12:00 m.	18	1.014

Total excretion: 900 C.c.

TABLE 25.—URINE EXCRETION AND WEIGHT IN CASE 11

Date	Intake	Excretion	Weight
March 4	600	400	31^{8}
March 6	500	150+	30^{8}
March 7	500	470	30
March 13	500	350	32^{3}
March 17	500	400	32^{4}
March 21	560	550	32^{3}
March 27	800	750	32^{12}
March 31	660	700	31^{13}
April 2	855	540	32
April 3	720	750	33
April 9	510	800	33^{4}
April 10	540	800	32^{13}
April 16	500	250	31
April 23	500	225	31^{12}
May 1	500	500	31^{11}
May 8	500	325	32
May 9	500	350	32

Blood Chemistry: Serum, milky; urea nitrogen, 16.8; nonprotein nitrogen, 32.2; uric acid, 2; creatinin, 1.3; cholesterin, 0.696; carbon dioxid, 43.3.

April 26: Child still improving; up in chair. Weight, 31 pounds and 12 ounces.

Blood Chemistry: Urea nitrogen, 16.8; nonprotein nitrogen, 46.9; uric acid, 2.4; creatinin, 1.2; cholesterin, 0.424 per cent.; total serum protein, 6.2 per cent.; serum sodium chlorid, 5.9 mg.

Urine: Albumin, two plus; occasional granular casts.

Blood pressure, 105/85.

May 10: Discharged with the following note: Free from edema. Water excretion about the same as intake. Urine: albumin, two plus, with only a rare cast.

Diet: 500 c.c. of fluid—water and milk—rice or other cereal, potato, vegetables, ice cream. Weight, 32 pounds.

Return Examination.—November 15: Since discharge from hospital six months ago has had frequent puffiness of the face, but no edema of legs or ascites. Has been on above diet since discharge. Has passed about 12 ounces of urine a day.

Physical Examination.—The child is in fairly good condition; pale; some edema about the eyes. Lungs: little dulness at left base. Heart: not enlarged. Abdomen: no ascites. Lower extremities, no edema. Blood pressure, 89.60.

Laboratory Examination.—Urine: Specific gravity, 1.030; albumin, heavy trace; rare casts. Blood Chemistry: Serum, milky; urea nitrogen, 14; uric acid, 2; creatinin, 1; cholesterin, 0.376 per cent.; total serum protein, 4.2 per cent.

CASE 13 (Hospital No. 214516).—Male, aged 4½ years, admitted Oct. 27, 1921. Observed one month in hospital with a previous history of five weeks. Only possible etiology was tooth extraction. The intractable edema despite marked limitation of fluid, the normal blood nitrogen, the high cholesterin, the lowered basal metabolism and the urine findings lead us to classify this case as a true nephrosis. A high protein diet tried for two weeks had no effect.

Family History.—Negative

Previous History.—Child frequently had fairly sore throat. Tonsils and adenoids removed two years ago. Measles, two years ago; pneumonia and otitis media, five months ago.

TABLE 26.—URINE EXCRETION IN CASE 13 BEFORE AND AFTER WATER TEST

Nov. 4, 1921. Water Test: Intake, 350 C.c.

Time	Volume, C.c.	Specific Gravity
8:30 a. m.	70	1.028
9:00 a. m.	55	1.006
9:30 a. m.	75	1.002
10.30 a. m.	16	1.006
11:15 a. m.	20	1.012
12:00 m.	6	
2:00 p. m.	10	
3:30 p. m.	15	1.020
2:15 a. m.	75	1.032

Total four hours, 242 c.c. Total twenty-four hours, 342 c.c.

Present History.—About five weeks ago had a tooth extracted. Almost immediately after that it was noticed that child had puffiness of eyelids, but in the course of two weeks it had disappeared. About ten days ago the edema reappeared and rapidly involved the body and the extremities.

Physical Examination.—Child chronically ill. General anasarca. Face: edematous. Eyes: almost closed; swelling of the lids. Throat: slightly congested. Lungs: little flatness and diminished breathing at right base. Heart: negative. Abdomen: distended with fluid wave. Marked edema of scrotum and penis. Extremities: marked edema.

Laboratory Examination.—Pirquet and Wassermann test, negative. Hemoglobin, 90 per cent.; erythrocytes, 5,470,000; leukocytes, 17,000; polymorphonuclears, 73 per cent. Blood pressure, 98/68.

Urine: albumin, four plus; many casts and a few white blood corpuscles.

Blood Chemistry: Serum, clear; urea nitrogen, 12.6; nonprotein nitrogen, 32.9; creatinin, 1.2; cholesterin, 0.552 per cent.

Phenolsulphonephthalein Test (intramuscular): Excretion first hour, 12 per cent.; second hour, 8 per cent.; total, 20 per cent.

Diet: Milk, 500 c.c. for four or five days; later reduced to 350 c.c. Weight, 37 pounds and 6 ounces.

November 8: Given thyroid, ½ grain, twice a day. Discontinued after two days.

November 11: Phenolsulphonephthalein Test (intravenous): Total excretion, 50 per cent. after two hours.

November 13: Child had not improved. Weight, 5 pounds more than on admission. Put on high protein diet, consisting of 350 c.c. skimmed milk; two eggs; chicken, 50 gm.; peas, 20 gm.; farina once a day.

November 14: Southey tubes applied to lower extremities; about 60 c.c. of edema fluid obtained. Analysis of edema fluid: specific gravity, 1.005; cholesterin, 0.012 per cent.; sodium chlorid, 0.643 per cent. Basal metabolism, 20 per cent. Blood pressure, 80/60.

CASE 16 (Hospital No. 210059).—Male, aged 2, admitted May 9, 1921. Child has had edema for eight months. Etiology, probably scarlet fever. Has had all modes of treatment, protein free diet, high protein diet, diuresis, thyroid, decapsulation of kidney, without any effect. The urine always contained large amounts of albumin and casts; the blood urea became high during the latter part of the illness. The cholesterin always remained high, but what was most surprising, the serum protein was not decreased. Child finally died. A typical case of nephrosis.

TABLE 27.—URINE EXCRETION AND WEIGHT IN CASE 13

Date	Intake	Excretion	Weight
October 28	...	315	37[6]
October 29	...	300	
October 30	...	60	
October 31	...	270	
November 1	690	120	
November 2	830	200	
November 3	600	300	42
November 4	360	300	
November 5	550	240	
November 6	600	180	
November 7	300	360	
November 8	30	18	
November 9	30	36	
November 10	390	150	42[2]
November 11	360	210	42[3]
November 12	360	90	
November 13	300	420	42[8]
November 14	360	240	42[12]
November 15	390	240	42[14]
November 16	423	150	43[4]
November 17	330	?	43[5]
November 18	360	?	44
November 19	420	420	45[2]
November 20	450	120	45[3]
November 21	270	270	45[4]
November 22	480	210	45[10]
November 23	350	200	45[11]
November 24	350	85+	46
November 25	350	239+	46[2]
November 26	350	150+	47
November 27	...	...	47[2]

Family History.—Three children. Mother had three miscarriages after birth of second child; otherwise negative.

Previous History.—Whooping cough when 7 months old; when 1 year old, fairly severe burn on body which healed in three weeks.

Present History.—About six weeks before admission an older sister of patient had scarlet fever. About this time this child had a mild rash for one day with temperature. One month before admission child fell a great deal, and it was then noticed that his legs were swollen and that he passed very little urine. Urine examined and albumin found but no blood.

Physical Examination.—Patient acutely ill. Generalized edema. Eyes almost closed because of swelling of lids. Ears: purulent discharge from right ear. Throat: tonsils ragged; not congested. Lungs: dulness at both bases. Heart: not enlarged. Abdomen: very much distended with shifting dulness. Extremities: swollen. Weight, 29 pounds.

Laboratory Examination.—Hemoglobin, 74 per cent.; erythrocytes, 5,500,000; leukocytes, 15,400; polymorphonuclears, 60 per cent.

May 9: Urine: specific gravity, 1.030; albumin, four plus; many hyalin and granular casts and rare leukocytes.

Blood Chemistry: Urea nitrogen, 18.2; uric acid, 1.5; cholesterin, 0.376 per cent.; carbon dioxid, 34.7; sodium chlorid, 5.5; serum protein, 5.77 per cent.

Pirquet and Wassermann tests, negative. Blood pressure, 90/60.

Diet: Water, 500 c.c.; sugar, 90 gm.

May 13: Put on high protein diet. Southey tubes were inserted in lower extremities. For next few weeks no improvement in the edema. Blood Examination: Urea nitrogen, 32.2; nonprotein nitrogen, 66.5; uric acid, 2; creatinin, 1.6; cholesterin, 0.532 per cent. Plasma Volume: cells, 24 per cent.; plasma, 76 per cent. Weight, 32 pounds.

June 9: Transferred to surgical service where double decapsulation of kidneys was done. Kidneys, large and pale.

June 25: Transferred to medical service. During stay in surgical ward there was not much change in the edema. Fundi were normal. Blood Chemistry: Urea nitrogen, 23.8; cholesterin, 0.308 per cent. Diet: fruit juices, vegetable, milk, 800 c.c. Within next few days child became very edematous. Diet consisted of 350 c.c. of milk.

July 11: Thyroid, ¼ grain, three times daily, given. One week later gelatin and cream cheese added to diet. This was followed by diarrhea, but edema became less marked. Urine could not be measured, but child was voiding a fair quantity. Two weeks later edema again increased. Put back on high protein diet and 10 grains urea chlorid, given three times a day. Weight, 25 pounds.

August 24: Blood Chemistry: Urea nitrogen, 47.6; cholesterin, 0.360; protein, 7.15 per cent.

September 3: No improvement. Given diuretic.

September 14: Paracentesis, 300 c.c. fluid obtained. Previous diet discontinued; put on 400 c.c. milk.

September 19: Put back on high protein diet.

September 30: Taken home against advice with no improvement. Urine remained the same throughout the entire stay in hospital, containing albumin, four plus, and casts but no blood cells. Discharge weight, 23 pounds, 5 pounds less than upon admission.

A few days later child was taken to Babies' Hospital, New York. No improvement. Child was transfused but died within two weeks.

ORAL DISORDERS IN PEDIATRICS*

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The responsibility of oral diseases must rest on the physician rather than on the dentist, for the dentist and oral surgeon heal and correct already existing oral disorders, while the opportunity of detecting and preventing potential disturbances comes to him whose contact with the patient commences early and continues with more or less frequency.

This is particularly true of the pediatrician; who visiting the patient in most cases shortly after birth assumes the care of the general condition, which naturally thrusts on him the responsibility for the condition of the oral cavity. The widespread interest lately aroused by statistics indicating the large numbers of children affected with teeth disorders, makes it desirable for the pediatrician to become better acquainted with the normal oral cavity, so that he may detect earlier any abnormal conditions or tendencies in the child's mouth. With these facts in mind, it may be profitable to examine anew some of the more common oral disorders.

Formation of Teeth.—Preparation for tooth formation takes place as early as the sixth week in utero, and between the seventh and eighth week, the first step in development is evident by the formation of what is known as a dental band or ridge. The enamel begins to form on the deciduous teeth about the seventeenth week in utero and ends about six months after birth.[1] It is evident, then, that the pediatrician has almost no control of the formation and general condition of the deciduous teeth. The condition of the primary teeth is practically settled before birth.

The formation of the teeth of the unborn child may be impaired in one or two ways: (1) by lack of suitable material with which to form teeth, and (2) by impairment of formation by toxemias. It is obvious that the fetus needs the salts of calcium and phosphorus in the formation of teeth, and it must depend on its mother for that supply. Vitamins are most essential so that their salts may be utilized. Therefore, besides other essentials necessary to attain proper metabolism, the mother should have a well balanced diet, giving special attention to those foods which contain mineral salts and vitamins if good deciduous teeth are to be formed.

Although the tissues of the mother, rather than the tissues of the unborn child, suffer from any acute or chronic toxemias, nevertheless these toxemias probably cause serious impairment of the formation of

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tissue because of its disturbances of metabolism, and consequently lessened assimilation of food. This naturally includes a diminution in the amount of available salts to be utilized in the formation of teeth. Another result of toxemia which also leads to a defective formation of teeth is anorexia. Hence it is important that all sources of toxemia in the mother should be eliminated as far as practicable. Dental decay often leads to toxemia in pregnant mothers. Only a small percentage of these mothers state that they received any treatment for dental decay. Of course, it would be far better if these pathologic dental conditions were discovered and treated before pregnancy occurred. Nevertheless, pregnancy is no barrier to dental treatment. About 75 per cent. of the mothers of the children attending the preventive clinic give a history of some dental ailment. With the exception of decayed teeth, most of these ailments disappear at the birth of the child, and reappear with subsequent pregnancies.

Dr. Percy Howe's animal experiments in the research laboratory of the Forsyth Dental Infirmary, have shown that lack of proper diet has some bearing on dental ailments, particularly when the teeth begin to loosen. Perhaps, the loosening of teeth may be the result of a drain by the fetus on the maternal supply of phosphorus and calcium. If this supply is not furnished through the diet of the mother, it is natural to assume that the maternal tissues, particularly the teeth and bones, will suffer, since they will be required to contribute the necessary elements for the bone and teeth formation of the unborn child.

Of the permanent teeth, the enamel begins to form at birth or shortly before birth with the first molar, and the complete formation of the enamel of all the permanent teeth is complete about the twelfth year on the crown of the third molar. After the fifth year, however, only the second and third molars have the formation of their enamel completed.[1]

The formation of teeth, both temporary and permanent, is subject to many disturbances, particularly those of infection and nutrition. The temporary teeth, as compared with the permanent teeth, show very little defects in their formation.

The formation of enamel proceeds at fairly regular intervals. Any temporary cessation of this process can usually be recognized, even to the time of occurrence, by noting the various defects in the enamel of the teeth undergoing calcification during that period. The effect of malnutrition on the teeth shows itself through many defects. Since the enamel is derived from the epithelium, and is also ultimately derived from the epiblastic germ layers,[1] the eruptive diseases, notably scarlet

1. Endleman, O., and Wagner, R. F.: General and Dental Pathology, St Louis, C. V. Mosby Company, 1920.

fever and measles, leave their imprint on the enamel of the teeth. In fact, any febrile condition of more than three or four days' duration seems to leave its mark on the formation of the enamel. Defective enamel formation usually occurs in rickets.

Such defects as the chalky appearance of the enamel, pitting, transverse bands on the surface, brown staining of the enamel, irregular and serrated edges of the teeth, are seen with very great frequency at the clinics. These are the result of constitutional diseases and malnutrition.

Dentition.—There is altogether too great a tendency on the part of the pediatrician to disregard the diagnosis of dentition. Dentition or teething should be regarded as a physiologic process and should proceed without any disturbances. Clinical evidence, however, does not always support this view. Unfortunately, a diagnosis of "teething" is often made either from neglect to perform a complete physical examination, or from inability to interpret properly the findings of such an examination.

H. Able states that a connection between febrile affections and dentition does not exist, but many febrile diseases lead to an increased eruption of teeth, in the same way as the increased growth of children occurs during or after febrile disorders, through the stimulating action of toxins on the epiphysis. He made observations on nineteen cases of measles in children under 2 years of age who showed an extraordinary increase of erupted teeth during the time of febrile attack and immediately afterward.[2]

There is an abundance of clinical evidence to show that the diagnosis of dentition can be made correctly in many instances. Kirk[3] states that the harmonious synchronism between root growth and tissue absorption is a delicately balanced mechanism, and a sort of moving equilibrium depending for its stability on the nutritional and physiologic balance of the entire organism. There is harmonious correspondence between the addition by growth to the developing root of the teeth and the absorption of the tissues overlying the tooth crown as the eruption of the tooth proceeds. Pain, which is a frequent accompaniment of teething, although this is difficult to prove, is caused not by pressure of the tooth on the gums, but rather by the pressure of the gums on the tooth, which, in turn, presses on the underlying nerves.

The evidences of teething may vary. Symptoms such as rise in temperature, disturbed sleep, gastro-intestinal disturbances (particularly diarrhea), increased salivation and increased desire for water, are common. The weight curve may be disturbed. In babies who show

2. H. Able: Wien. klin. Wchnschr., No. 14, 1919, p. 392.
3. Kirk, E. C.: Dental Cosmos **62**:1373 (Dec.) 1920.

evidence of spasmophilia, convulsions are very common with teething. Often babies who previously offered no resistance to examination of the mouth will, when teething, oppose any attempt to open the mouth for examination, keeping the lips very firmly compressed. The gums in the areas where teeth are to be erupted are tender and may appear slightly swollen, either red or, more often, white in color. The baby frequently has a desire to bite on anything, and finds relief in this way. This tendency disappears when the teeth are erupted. Otitis media and bronchitis are said to be frequent accompaniments of teething; this may be due to a lowered resistance caused by physical irritation. It is commonly accepted that physical irritation from adenoids, phimosis and pin worms may cause constitutional disturbances. These disappear with the removal of the cause, and may be favorably compared to the disappearance of the symptoms after the teeth erupt. Dentition may sometimes have a marked effect in increasing the irritability of the nervous system, more especially in infants having rickets, spasmophilia or some nervous disorders.

The evidence that these symptoms are due to dentition alone is, first, that the symptoms disappear, often with remarkable suddenness, immediately after the teeth erupt, and second, that with the eruption of other teeth, similar symptoms appear.

Hygiene of the Mouth.—Oral disorders, especially in the first months of life, frequently result from practices which are thought to be required by good hygiene. The epithelium of the mouth of the infant in the early months is very sensitive to trauma. Even the slightest trauma may be followed by infection. It has been demonstrated repeatedly that infants who do not receive any mouth cleaning before the eruption of the first tooth show a healthy epithelium and do not suffer the various forms of stomatitis peculiar to early infancy. No matter how carefully the finger is introduced into the mouth for cleansing purposes, nothing but harm can possibly result from such practice. A toothless mouth requires no cleansing.

Trauma plays an important part in the etiology of stomatitis occurring during infancy. The giving of food which is too hot or unclean also causes stomatitis. If more attention were paid to proper cleansing of nipples, and to avoidance of the introduction of soothers and other unnecessary objects into the mouth, there would be fewer cases of stomatitis in infancy.

The principles of the hygiene of the mouth containing teeth are still uncertain. The doctrine that a clean tooth never decays is not borne out by clinical evidence. It may be nearer the truth to state that a clean tooth may not decay as rapidly as one that is not clean. Tooth powders and pastes, mouth washes and alkaline dentifrices, and other cleaners, chemical or mechanical, are recommended by many authorities

for the prevention of oral disorders. It has been shown that antiseptic washes act only while they are in the mouth, if they act at all; five minutes after their use cultures show growth.[4] Weak acid washes act to better advantage than alkaline washes by increasing salivary secretion. Antiseptic washes, on the other hand, are salivary depressants.[4] As far as tooth powder and tooth pastes are concerned, there is no direct evidence to support the claims that they prevent decay. Cameron [5] has shown that a well shaped tooth has no food residue ten minutes after soft pultaceous food has been consumed. It is the belief of some dental authorities that teeth are self-cleansing. Many uncivilized peoples have clean teeth despite the fact that they have never even seen a tooth brush. Some of these people rub their gums with the fingers or cause friction on their gums mechanically by choosing foods that require a great deal of mastication. Some barbarians who are said to eat very soft mushy food, and eat only twice daily, have clean oral cavities. This may be explained by the fact that their foods contain an abundance of vitamins and are well supplied with salivary activators.

Carious Teeth.—There is hardly any one factor more striking today than the marked prevalence of carious teeth among civilized people. The fact is all the more remarkable in that as soon as civilization creeps into any community hitherto without its blessings, the number of those affected with carious teeth greatly increases. Statistics have demonstrated how vitally carious teeth affect the nation. Dental defects were second in importance as a cause for physical rejection in the United States Army. This is a sorry showing that cannot be laid entirely to the dental profession. The fact that school records show that toothache is one of the most frequent causes of absence,[6] suggests the seriousness of the situation. In the children's clinics of every city, the presence of a child having a well formed set of teeth with little or no caries, or only one or two teeth missing, usually excites comment from the examiner. I have reviewed the literature on carious teeth, and have been surprised to learn how little is known about the prevention of caries. Hipprocates, in 500 B. C., wrote that caries is a manifestation of stagnation of depraved juices. Other causes such as inflammation, worms, putrefaction, chemical disolution, parasites, drugs, decomposition, various kinds of foods,[7] micro-organisms,[8] and osmosis [9] have been considered at one time or another since then. In 1881-1901 the chemico-parasitic theory of Miller seemed to have settled beyond doubt to most

4. Pickerill, H. P.: The Prevention of Dental Caries and Oral Sepsis, London, Bulliere, Tindall and Cox, 1919, p. 265.
5. Cameron, H. C.: Lancet **1**:86 (April 23) 1921.
6. U. S. Public Health Rep., Nov. 19, 1920, p. 2763.
7. Baker, A. W. W.: Tr. Roy. Acad. Med., Ireland **10**:355, 1891.
8. Walkhoff: Brit. J. Dent. Sc. **64**:212 (July) 1921.
9. Echerman, R.: Dental Items of Interest **40**:466 (June) 1918.

members of the dental profession that the cause of carious teeth had been solved, and henceforth prevention of caries was a comparatively simple process, i. e., by the removal of the cause of fermentation locally. This theory has been convincingly disproved by Howe and others.[10] It is due to the persistent efforts of Drs. J. Sim Wallace and H. C. Pickerill [4] of England and Drs. Percy Howe and W. J. Gies of this country that the theory of diet being a controlling element in the causation of carious teeth is gaining support. Other influences may be responsible for the increase in the number of carious teeth, such as environment, manner of living, and infection. The evidence, however, seems to point toward defective diet as being largely responsible for the widespread prevalence of carious teeth.

The following, gathered from the literature on carious teeth, are the usual illustrations which point to diet as a causative factor of caries:

1. Teeth of primitive people in Australia, who for many years have lived under civilized or partially civilized conditions, are bad in comparison with those of their tribe who have continued under primitive conditions.[11]

2. Kaffirs supplied with the food of civilization have in one generation become totally different, in regard to caries, from those Kaffirs who are still living on their native diet.[1]

3. The disease is rare among the Red Kaffirs in southeastern Africa who have not taken kindly to European conditions and diet.[12]

4. The Esquimaux were practically free from caries until change of diet with the influx of refined food.[10]

5. Colyer notes that men of certain tribes of Africa did not have dental caries until they were recruited into the British Army.[13]

6. The Maori children in New Zealand have the very low rate of 1 per cent. caries. In Europe the rate for carious teeth is 85 per cent.[14]

7. In Scotland, among those living on the highlands and using coarse foods, caries is rarely seen. Those who inhabit the lowlands and partake of the finer foods suffer far more from carious teeth.[15]

At a clinic held in June, 1921, during the annual meeting of the American Medical Association, at the Forsyth Dental Infirmary, Dr. H. DeW. Cross presented 176 immigrant children of all ages, all of whom had been in this country less than four weeks. Almost all nationalities were included in this group, except those of English, Irish or French descent. Virtually none of these children had ever seen

10. Howe, P.: Dental Cosmos **42**:921 (Aug.) 1920.
11. Suk, V.: Am. J. Physical Anthropol. **2**:351, 1919.
12. Colyer, S.: Brit. Dent. Rec. **39**:401, 1919.
13. Colyer, S.: Brit. Dent. Rec. **37**:405, 1917.
14. Gibbs, J. H.: Edinburgh M. J. **18**:433 (June) 1917.
15. Wells, F. M.: Brit. J. Dent. Sc. **14**:135 (May) 1921.

a toothbrush. Dr. Cross found that 30 per cent. had perfect mouths, 30 per cent. had no more than two small cavities, and a bad mouth was the exception among the remainder. In contrast to this, I presented almost an equal number of children, of about the same ages, all being born in this country. They showed little or no evidence of malnutrition and had been chosen at random, just as were those of the other group. In this group a perfect mouth was the exception; about 80 per cent. of these children showed mouths in need of dental treatment. A few of the mouths were almost beyond repair. A large proportion of these children had been under a physician's care since birth. Needless to mention, these school children were well versed in the art of using the tooth brush, and a great majority of them presented the so-called physiologically clean mouth, but had carious teeth, while many of the "new Americans" of Dr. Cross's group had tartar on their teeth, but were free from caries.

Since our knowledge of etiology of caries is insufficient for its prevention, early treatment is of paramount importance. It has been conservatively estimated that more than 90 per cent. of the children entering the public schools are in need of treatment for carious teeth. No doubt, a large proportion of these children had already been seen, for one reason or another, by a physician, and caries noted yet comparatively few show any evidence of dental treatment. Instead of early decay being arrested, the condition is allowed to go from bad to worse.

Early decay is first seen at the junction of the teeth and gums. If the pathologic condition of the teeth is so far advanced that the tooth does not function, then extraction is strongly advisable. A badly decayed tooth does not function because the child will not chew on it, to avoid the pain caused by the exposed pulp. This leads to bolting the food. Extracting badly decayed temporary teeth conserves the permanent teeth which are in the process of formation, and inflammation around the apex of deciduous teeth will lead to permanent changes in the secondary teeth directly underneath.

Discussion of the necessity for treatment of deciduous caries would be unnecessary were it not for the fact that its treatment is sadly neglected and postponed. Mothers are asking for treatment of their children's first teeth, only to be told that it is impractical and inadvisable because these teeth are only temporary, and are soon to be replaced by permanent ones. Sometimes, the excuse given for not extracting decayed deciduous teeth is that the jaw will not develop properly. These and many other unwarranted excuses are being given to mothers daily both by the dentist and the physician. It is the opinion of those who are in the best position to judge, that any harm that may possibly result from the extraction of carious deciduous teeth is negligible, in

comparison to the harm resulting from the failure to extract. Since no child is too young to have caries, it follows that no child is too young for treatment.

No cavity is too small to be disregarded, and the pediatrician should insist on the immediate treatment of caries at any age. It is only by taking care of the teeth of children of preschool age that the teeth of the school children and adults will be safeguarded. The time may be approaching when public schools will demand as necessary for admission a certificate of a clean mouth requiring no dental treatment.

The pediatrician should be aware of the fact that conditions existing during the period from birth until the sixth year determine the future condition of the teeth, all the teeth being already in formation, except the second and third molars, which are formed after this period. In other words, the question as to whether the child's teeth may become carious is practically settled before the eruption of the first permanent tooth, which occurs at 6 years. It is not generally recognized by the pediatrician that the first years of a child's life are critical ones as far as structure of the permanent teeth are concerned.

Diet and exercise of the jaws and teeth are essential, more especially under 5. Dr. W. J. Gies [16] states that since the teeth are formed principally from the salts of calcium and phosphorus, these salts should be given in sufficient quantities in the diet so that teeth will develop as they should. Dr. Percy Howe [17] emphasizes that in order that the body may be able to assimilate the calcium and phosphorus, vitamins are a very necessary addition to the diet. Mrs. May Mellanby suggests [18] that fat soluble A or some other vitamin of similar origin is essential to the diet, before calcium can be used to the extent necessary for the construction of normal teeth and jaws. Dr. J. Sim Wallace insists that the teeth and jaws be made to function through mastication.[19] He believes that soft, mushy foods do not exercise the jaws sufficiently nor stimulate the gums, and that food which requires mastication causes friction in the gums and produces a hard healthy condition. Besides urging that food be hard enough to cause vigorous mastication, Pickerill advocates the use of food that will increase salivary secretion.[4]

Although no one factor can account for the prevalence of caries, it seems reasonable to suppose that the dietary solution of the problem of carious teeth centers about:

First.—The daily intake of foods that contain those substances from which teeth and jaws can be formed, namely, sufficient calcium and phosphorus.

16. Gies, W. H.: Dominion Dent. J. **33**:163 (May) 1921.
17. Howe, P.: Dental Cosmos **63**:1086, (Nov.) 1921.
18. Mellanby, M.: Brit. J. Dent. Sc. **64**:70 (March) 1921.
19. Wallace, J. S.: Brit. Dent. J. **32**:415, 1911.

Second.—Adding vitamins to the diet so that the body may be able to utilize these elements. Fortunately, foods that contain an abundant supply of calcium and phosphorus usually contain vitamins also.

Third.—The development and proper functioning of the jaws and teeth, which can best be accomplished by vigorous mastication, therefore, hard and fibrous foods are desirable in the diet.

Fourth.—The stimulation of salivary secretion is necessary if the teeth are to be assured of any benefit that may come from a copious flow of saliva; this can be best accomplished by including in the diet foods that are classed as salivary activators.

A great deal of mineral matter is lost by the methods of preparation in cooking. After vegetables are boiled, the water containing a good deal of the mineral salts is usually discarded. Cereals are ground fine, by high milling, which causes the removal of mineral matter by the finer machinery. White bread, which is made of fine flour, is used extensively instead of common whole wheat bread. These, and many other illustrations show that our modern dietary fails to meet the vital needs of the body.

The preventive clinic at the Forsyth Infirmary recommends cereals such as Irish oatmeal, rolled oats, cracked wheat, cracked corn, hominy grits, brown rice, and others for common usage. There is less destruction in them of the very valuable minerals, and they require more thorough mastication.

As substitutes for the commonly used bread made of fine white flour, the use of whole wheat, rye, bran and oatmeal breads is strongly advocated for their coarser qualities. Rye and whole wheat flour are recommended for home baking. In place of the finer sugars, molasses, honey and pure maple sugar can be substituted to advantage.

Animal experiments have proved that calcium is indispensably necessary to teeth formation. Children who inhabit regions that have excessively soft water show an excessive number of cases of caries.[20] Children living in regions with water containing calcium salts, carbonates or sulphates, have much better salivary glands than those who have grown up in soft water regions; also, the former have less caries than the latter.[21]

Howe has demonstrated that caries can be prevented and arrested by diet alone.[10] By feeding animals with a diet deficient in vitamins, caries and decay readily follow. He has shown, also, that the teeth are one of the first and sometimes the only tissue to be affected by a diet deficient in antiscorbutic vitamins. Vitamins themselves do no apparent good so far as the teeth are concerned if there is an insufficient amount of calcium in the food.

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20. Cook, J. B.: Lancet **1**:888 (March 28) 1914.
21. Rose, C.: Deutsch. Monatschr. f. Zahnh. (Jan.-Aug.) 1908.

Wallace has reported very favorable results in prevention of caries in children by giving a diet containing hard foods. The children developed strong jaws as a consequence of repeated functioning of the masticating apparatus.

It is highly probable that saliva contains a substance or substances to prevent either the onset or the progress of caries. It is interesting to note that saliva of mouths having good teeth has a higher percentage of calcium than saliva of mouths having caries.[4] This may be another means of determining whether or not the body is able to fulfill its calcium requirements. It may not be out of place here to compare calcium deficiency in saliva to endocrine insufficiency. By that is meant that if the body is not supplied with a sufficient amount of calcium, either because of insufficient intake or through a failure of the body to utilize the ingested calcium because of some disturbance in metabolism, the saliva may be taken as an indicator, to some extent, of the calcium content of the body. Likewise, if there is a dietary deficiency, there is every reason to expect a deficiency in the functioning of all the glands of the body. This deficiency includes an endocrine insufficiency, since in proportion the more highly specialized tissues are usually the worst sufferers in any constitutional disturbances. Assuming, therefore, that the body has a sufficient supply of available mineral salts, the mouth can best be supplied with these through stimulation of its gland products, that is, through stimulating the secretion of the salivary glands.

The more saliva that can be stimulated in a natural manner, the more probable it is that there will be sufficient protective agencies. The most natural salivary stimulants are foods, and the character and quantity of saliva depends on the character of food. The salivary secretion does not respond in the same way to all foods. For example, dry bread increases the amount of saliva two to one, apples and oranges increase the saliva six to one. Acids and highly flavored foods increase the saliva in quantity, alkalinity and ptyalin content. Probably all three have much to do with the cleansing of the mouth and prevention of caries. Almost all vegetables, cooked or raw, and all fruits stimulate the flow of saliva. Moreover, when these foods are eaten, the flow of saliva continues long after they are swallowed. The celluloses arrested in the mouth are disintegrated by the teeth; the acidity, remaining long enough in the mouth after the food has been swallowed, is strong enough to continue to simulate the flow of saliva. Other food stuffs besides fruit and vegetables that may be classed as salivary activators are crusts of bread, toast, zwieback, coarse biscuits, nuts, vinegar, sardines and salads. Foods that are known to be poor salivary stimulants include farinaceous foods, fine white bread, fine white biscuits, tea and coffee, alkaline foods, sweets, chocolate, manufactured

sugar and tasteless food. Foods classed as indifferent to salivary stimulation include meat, fish, eggs, rice and brown bread.[22]

It has been stated that caries has increased with the increased consumption of refined sugar and commercial glucose used in jams, sweets and syrups. Curiously, these are known to be salivary depressants. According to Wheatley, between 1919-1920, children from Shropshire, 5 years of age, showed on an average 1.9 decayed teeth per child, as against 6.4 per child between 1910-1914. This seemed to be explained largely by the restriction in the purchase of carbohydrates and by the fact that new bread was prohibited and crusts of coarse bread had to be eaten. In poor districts a half penny worth of raw carrot (a vegetable particularly rich in vitamins) largely replaced the prewar penny worth of sweets.[23]

At the preventive clinic a suitable diet is prescribed according to the digestive capabilities of the child, which includes a sufficient amount of calcium and phosphorus, foods containing vitamins, coarse foods that require vigorous mastication, besides foods which are salivary activators. In order to make these foods more palatable and digestible, an expert dietician is to present practical demonstrations in the art of cooking to the mothers. Children frequently refuse to eat fruit, vegetables, and other foods which are most essential for their food values in addition to their salt and vitamin content. This difficulty is largely due to the inability of the mother to make the food attractive or palatable enough to tempt the child's appetite. In addition, this demonstration will have economic value since it stresses food conservation and recommends only the use of foods in season.

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22. Baldwin, H.: Brit. Dent. J. **17**:218 (March 11) 1921.
23. Hendley-Read, E.: Dent. Rec. **41**:185 (April 19) 1921.

AN EPIDEMIC OF STREPTOCOCCUS HEMOLYTICUS SEPTICEMIA *

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The purpose of this report is to record an epidemic of streptococcus septicemia occurring late in November and early in December, 1921, in a ward of seventeen babies in a nursery home.

The age of these infants ranged from one month to 7½ months. They were housed in a new building in a commodious ward, well ventilated and well lighted, with a sun porch attached, where they spent the day in individual cribs and were returned to their beds in the ward at night.

Before the onset of the epidemic all the babies were in good general condition, gaining in weight and having no gastro-intestinal disturbance. All were bottle fed babies, on whole milk dilutions with water and sugar added. Two were receiving small amounts of breast milk in addition to their cow's milk formulas. The milk and water used was boiled three minutes.

Suddenly, as it were out of a clear sky—two of the youngest infants (aged 1 month and 2 months, respectively) began to have fever, one 103 F. and the other 104 F. For the next two days their temperatures ranged from 103 to 105 F., coming down to 102 F. on the fourth day—the day of their death.

Clinically, both children showed extreme prostration, an acutely inflammed pharynx, enlarged cervical glands; on the third day distention of the abdomen with paralysis of the intestines; stupor and death on the fourth day. One infant showed some retraction of the head on the third day. There was no vomiting and no diarrhea. Enemas were given daily. Both infants took their food eagerly until the day of death. There were no convulsions. Nothing abnormal was found on examination of the heart and lungs.

The necropsy findings were: Case 1: Septicemia; peritonitis; cloudy swelling of viscera; hypostatic congestion of lungs and pericardial effusion. Case 2: Septicemia; cloudy swelling of viscera; punctate hemorrhage of renal capsule with a little bloody fluid in the peritoneal cavity.

During the next two and one-half weeks, seven other infants developed symptoms and clinical findings similar to the above, but with the absence of the extreme prostration, the marked pharyngitis and

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* From the Department of Pediatrics, University of Oregon Medical School.

cervical adenitis. Five of these seven infants died, and at necropsy the picture was the same as in the first two cases recorded. The degree of pathologic change seeming to be directly proportional to the duration of the illness (Table 1).

Blood was taken from the longitudinal sinus in six of the cases and cultured in sugar agar and sugar bouillon. The *Streptococcus hemolyticus* was recovered in five cases. No attempt was made at further classification of the streptococcus other than to note that it

TABLE 1.—NECROPSY FINDINGS

	Case						
	1	2	3	4	5	6	9
Septicemia	+	+	+	+	+	+	+
Peritonitis	+	..	+	+	+	+	+
Cloudy swelling of viscera	+	+	+	+	+	+	+
Bronchopneumonia	..	..	+	..	..	..	+
Hyperemia of lungs	+	..	..	+	+	..	..
Edema of brain	..	..	..	..	..	+	+
General lymphoid hyperplasia	..	..	+	+	+	+	..
Pericardial effusion	+	..	..	..	..	..	+
Punctate hemorrhage of renal capsule	..	+	..	..	..	..	..

belonged to the hemolytic group. Of the two infants who eventually recovered, one showed a positive and the other a negative culture. All of the seven infants that died and came to necropsy gave positive cultures of the *Streptococcus hemolyticus* from the heart's blood. In one case (Case 4) cultures taken from the heart's blood, pericardial fluid, pleural fluid and peritoneal exudate showed the *Streptococcus hemolyticus* in pure culture.

TABLE 2.—CLINICAL DATA

Case	Name	Age in Mo.	Fever	Prostration	Pharyngitis	Adenitis, Cervical	Distended Abdomen	Retraction of Head	Late Stupor	Leucocytosis	Blood Culture	Duration of Disease Days	Result
1	Gordon	1	+	+	+	+	+	+	+	..	..	4	Death
2	Marion	2	+	+	+	+	+	0	+	..	..	4	Death
3	Lena	1½	+	+	0	0	+	+	+	Slight	..	4	Death
4	Eleanor	3½	+	0	0	0	+	0	+	+	+	9	Death
5	Dean	4½	+	0	0	0	+	0	+	+	+	13	Death
6	William	4½	+	0	0	0	+	0	+	+	+	10	Death
7	Leo	4	+	0	0	0	0	+	0	+	0	6	Recovery
8	Martin	3½	+	0	0	0	0	0	0	+	+	10	Recovery
9	Norma	7½	+	0	0	0	+	+	0	+	+	5	Death

The leukocyte counts varied markedly in different patients and during the course of the disease in the same patient, without bearing any remarkable relation to the duration of the disease, the amount of prostration, or the ultimate outcome. These counts varied from 10,000 to 44,000 per cm. The average leukocyte count during the disease, as shown by thirty counts taken from seven patients was 22,650 per cm.

The average differential count taken soon after the onset of the cases was: Polymorphonuclear neutrophils, 52.6 per cent.; basophils,

0.3 per cent.; eosinophils, 0.3 per cent.; small mononuclears, 40.1 per cent.; large mononuclears, 3.1 per cent.; transitionals, 3.3 per cent.

A composite clinical picture of the disease may be summed up as follows:

An infant of the average age of 3½ months, previously well, has a sudden rise in temperature, moderately inflamed pharynx, leukocytosis of about 22,000, a blood culture positive for the *Streptococcus hemolyticus,* a distended abdomen, stupor occurring late (or not at all) and death intervening on about the sixth day of the disease. Cervical adenitis and retraction of the head may also be present (Table 2).

Other babies in the ward showed slight variation from the normal in their temperature records, but not enough to be classed clinically as having the disease. Only one blood culture in this group was taken and it was negative.

At the onset of the epidemic, throat cultures were taken from four of the sick infants and a pure culture of *Streptococcus hemolyticus* was recovered from three while the fourth showed a short gram-negative bacillus together with the *Streptococcus hemolyticus.* A vaccine was prepared from these throat cultures and administered as a preventive to the well babies and in the treatment of the sick.

The entire nursery was put under quarantine and a strict isolation of the sick was instituted at the onset.

Treatment was, in the main, symptomatic. Sodium-bicarbonate was given both by mouth and by rectum. Stimulation with camphor in oil, caffein and digitalis was used. Salt solution was not administered intraperitoneally owing to the ever present abdominal distention and the complicating peritonitis. In one case stock antistreptococcus serum (20 c c, subcutaneously, in two doses) was given without any apparent change in the clinical course of the disease. Both the well and the sick received small doses of the autogenous vaccine every other day. Its effect on the sick was not striking, but it is possible that the giving of this vaccine to the well babies may have aided them in building up an immunity to the disease.

An effort was made to determine the source of the infection. The milk cultured showed no *Streptococcus hemolyticus.* In addition it was the custom to boil all the milk and water used in feeding for at least three minutes.

Cultures were taken, separately, from the throat and nose of each adult (twenty-two in all) connected with the institution. They showed about the usual incidence of *Streptococcus hemolyticus* in the throats of normal adults. Only two persons showed an abundant growth of the *Streptococcus hemolyticus* from both the nose and throat. These two adults had no part in directly caring for the infants of this par-

ticular ward nor did they come in contact with their food supply. However, they mingled, when off duty, with those in direct charge of these infants at the onset of the epidemic. One of these "carriers" was removed from the nursery for a period of two weeks. Since her return (more than three months ago) there has been no new case. In fact, the whole epidemic from the beginning to the end was of only three weeks' duration.

To sum up the more striking features:

1. *The suddenness of the onset of an epidemic of Streptococcus hemolyticus septicemia in a ward of seventeen babies all of whom were previously in good physical condition.*—In 1918, when the *Streptococcus hemolyticus* came in for such strong incrimination as the great etiologic factor in respiratory infections, there were, as a rule, predisposing diseases of various sorts, such as measles, influenza and pneumococcus pneumonia, which broke down the resistance of the body and prepared the way for the invading streptococcus (MacCallum,[1] and Blake[2]). In the cases here reported no predisposing disease was present.

2. *The absence of vomiting and diarrhoea.*—These symptoms are frequent complications of all acute infective processes in infants, yet in this group of cases they were entirely absent.

Epidemics of diarrheal diseases due to the streptococcus have been reported (Wilson[3]).

One might suppose that harboring virulent streptococci in the throat, on swallowing these organisms a definite gastro-enteritis would result. Davis,[4] investigating experimentally the fate of the *Streptococcus hemolyticus* in the gastro-intestinal canal, showed that this organism does not develop appreciably in the intestine, nor does it readily gain a permanent foothold there.

3. *The absence of any apparent localized infection or site of primary infection.*—Exception to this is made in the case of the first two cases reported; both babies showed marked pharyngitis and cervical adenitis.

Fox and Hamburger,[5] reporting a streptococcus epidemic following measles, note that it would seem more likely that the process was a primary septicemia, although the infection atrium is clear in no case.

4. *The absence of pulmonary involvement, at least until very late in the disease.*—This, in spite of the fact that bronchopneumonia, as MacCallum[1] and Longcope[6] have reported, was so prevalent in the streptococcal epidemics in the Army camps in 1918.

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1. MacCallum: J. A. M. A. **71**:704 (Aug. 18) 1918.
2. Blake: Ann. Otol., Rhinol. & Laryngol. **28**:361, 1919.
3. Wilson: War Med. **2**:556, 1918.
4. Davis: J. Infect. Dis. **26**:171, 1920.
5. Fox and Hamburger: J. A. M. A. **70**:1758 (June 8) 1918.
6. Longcope: War Med. **2**:566, 1918.

5. *The generally good appearance of the patient until very near the end, thus belying the seriousness of the disease.*—Clinically, this possibly was the most striking feature, and were it not for the fact that positive blood cultures had been obtained, a good prognosis might have been given on the physical findings, when in reality the patient was near death. It leads us also to believe that many of our so-called ordinary "flu" infections are in reality septicemias.

6. *The uniformity with which positive blood cultures were obtained.*—In six patients, with clinical evidence of the disease in which blood cultures were taken, five, or 83 per cent., gave positive cultures for the *Streptococcus hemolyticus.*

Blanton, Burhans and Hunter [7] state:

> The infrequency of septicemia accompanying other localizations of streptococci in the body has frequently invited remark. On many occasions organisms have been recovered from blood at necropsy which repeated cultures had failed to reveal during life.

Davis and Rosenow,[8] reporting the Chicago epidemic of streptococcus sore throat in 1912, found that blood cultures were almost always negative.

Keegan,[9] reporting a hospital epidemic of streptococcic sore throat with surgical complications, obtained negative results from blood cultures.

Only one case of streptococcus septicemia was encountered by Nobécourt and Gimbert [10] with bacteriologic examination of the blood in 600 cases among 3,000 soldiers in more than a year.

Abderhalden [11] obtained 57 per cent. positive blood cultures in fifty cases of septicemia.

Longcope,[6] pointing out the relation of the *Streptococcus hemolyticus* to pneumonia in the troops in the United States, says that blood cultures gave no growth.

However, Wilson [3] reports obtaining the streptococci from blood cultures in twenty out of twenty-three cases.

7. *The marked uniformity with which peritonitis was encountered.*—Clinically this was manifested by a distended tympanitic abdomen, with late paralysis of the intestine, but without the characteristic vomiting and tenderness. It did not appear as an "acute abdomen."

MacCallum [1] says, in regard to the pathology of the epidemic of streptococcal bronchopneumonia in the Army camps, that "peritonitis occurred only twice."

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7. Blanton, Burhans and Hunter: J. A. M. A. **72**:1520 (May 24) 1919.
8. Davis and Rosenow: J. A. M. A. **58**:773 (March 16) 1912.
9. Keegan: J. A. M. A. **72**:1434 (May 17) 1919.
10. Nobécourt and Gimbert: Bull. Soc. méd. d. hôp. de Paris **41**:1037, 1917.
11. Abderhalden: J. A. M. A. **67**:236 (July 15) 1916.

Irons and Marine,[12] reporting on streptococcal infections following measles and other diseases, cite two cases occurring in the course of measles with primary peritonitis.

The only clear cut account of a case in a child found in the literature is that of a girl, 6½ years old, reported by MacLennan and McNee[13] in 1913, who had a primary *Streptococcus hemolyticus* peritonitis with septicemia. This occurred after an attack of measles and presented the clinical picture of an "acute abdomen." Operation was performed and a general peritonitis was found with a normal appendix. No localizing cause for the peritonitis was revealed. Pus from the abdomen and blood culture showed the *Streptococcus hemolyticus*. The patient recovered.

8. *The epidemiologic study.*—That pathologic streptococci of the hemolytic group can be conveyed by milk is common knowledge (Davis,[14] Jones,[15] Salter[16] and others). Milk was apparently not a factor in the spread of the present epidemic as a great many more children taking the same milk were not affected. Also, the cases did not have their onset simultaneously, and, finally, the milk used was always boiled and when examined bacteriologically gave negative cultures for the *Streptococcus hemolyticus*.

Davis[17] states that there is no evidence to indicate that strains of streptococci pathogenic to man can even resist the usual temperature for pasteurization (145 F. for thirty minutes).

Reviewing the recent literature which is fairly well saturated with bacteriologic studies of the *Streptococcus hemolyticus*, one is impressed with the frequency which the organism inhabits the throats of not only persons suffering from acute infectious diseases, but the throats of normal persons (Otteraaen,[18] Smillie,[19] Pilot and Davis,[20] Havens and Taylor,[21] and Pilot and Pearlman[22]).

In fact, Davis[23] states that cultures taken at short intervals sooner or later reveal the presence of hemolytic streptococci in the throats of virtually all normal adult persons. True, they are found less frequently

12. Irons and Marine: J. A. M. A. **70**:687 (March 9) 1918.
13. MacLennan and McNee: Brit. J. Dis. Child. **10**:258, 1913.
14. Davis: J. Infect. Dis. **23**:559, 1918.
15. Jones: J. Exper. M. **31**:347, 1920.
16. Salter: Am. J. Hyg. **1**:154, 1921.
17. Davis: Am. J. Pub. Health **8**:40, 1918.
18. Otteraaen: J. Infect. Dis. **26**:23, 1920.
19. Smillie: J. Infect. Dis. **20**:45, 1917.
20. Pilot and Davis: J. Infect. Dis. **24**:386, 1919.
21. Havens and Taylor: Am. J. Hyg. **1**:192, 1921.
22. Pilot and Pearlman: J. Infect. Dis. **29**:47, 1921.
23. Davis: J. Infect. Dis. **29**:524, 1921.

in the normal throat after tonsillectomy, as reported by Tongs,[24] Bryan,[25] Nichols and Bryan,[26] Van Dyke,[27] Pilot and Davis,[20] and Meyer, Pilot and Pearlman.[28]

However, Bloomfield,[29] reporting on the significance of bacteria found in the throats of healthy people, states that hemolytic streptococci of the typical beta type (pathogenic) were not obtained in any case.

This is of interest, as the cultures were made from people who were in intimate contact with patients suffering from sore throats due to these organisms. We believe that their presence in normal throats, as reported by some writers, indicates the recent presence of widespread infection among large groups of people with a virulent type of the germ.

These facts lead one to suspect that in the epidemic under study we were dealing with a different strain of hemolytic streptococcus than the ordinary throat inhabitant, or that the virulence of one of the streptococcus strains inhabiting the normal throat became activated and by contact infection (mainly hand infection, in the present case) was spread to other members of the ward.[30]

I wish to express my appreciation to Dr. Robert G. Hall for his courtesy in permitting me to study and report these cases, to Dr. R. L. Benson and Dr. F. R. Menne for the necropsy reports and for their study of the throat cultures of the adults, and to Huntley and Howe Laboratory for their cooperation in examining the blood cultures.

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24. Tongs: J. A. M. A. **73**:1050 (Oct. 4) 1919.
25. Bryan: Ann. Otol., Rhinol. & Laryngol. **28**:337, 1919.
26. Nichols and Bryan: J. A. M. A. **71**:1813, 1918.
27. Van Dyke: J. A. M. A. **74**:448 (Feb. 14) 1920.
28. Meyer, Pilot and Pearlman: J. Infect. Dis. **29**:59, 1921.
29. Bloomfield: Johns Hopkins Hosp. Bull. **32**:33, 1921.
30. At the present time (April 1922) Portland is having an epidemic of septic sore throat, undoubtedly due to contaminated milk. There have been several deaths among infants due to streptococci septicemia with terminal peritonitis.

BOOK REVIEW

HAUTKRANKHEITEN UND SYPHILIS IM SAUGLINGS UND KINDESALTER. An Atlas. Professors H. Finkelstein, E. Galewsky and L. Halberstaedter. Berlin, Julius Springer, 1922.

The authors give a brief but comprehensive summary of most of the skin diseases seen during infancy and childhood. Wherever possible, their plan has been to give a description of the skin lesion, followed by a discussion of the symptomatology, the general course of the condition and a differential diagnosis. They add a few words on prognosis and conclude with an outline of the treatment, both general and local, not forgetting to mention prophylaxis. The most important feature for the average physician, however, is the inclusion of numerous colored plates. Each condition described has its accompanying illustration and thus the practitioner is enabled to form a visual conception of the lesion. While it is impossible to duplicate exactly the finer shades of color or the minute details of configuration, still the representations are sufficiently true to life to recall immediately the disease. This volume will prove a valuable addition to any pediatrician's library.